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THE ELECTRIC STRAIN GAUGE BALLISTOCARDIOGRAPH

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SINCE the recording of the first ballistocardiogram by Gordon,[1] the recoils of the body from heart movements and circulatory impacts have been studied with various types of apparatus. Horizontal ballistocardiographs in the form of a bed or table have been suspended from the ceiling or some supporting framework[1-9] or supported upon steel strips.[10,11] Some, consisting of a chair or platform with spring supports, permit vertical recording.[12-15] Others have taken the form of a plank supported by rubber stoppers,[16] a platform suspended from the diaphragm of a drum,[17] a seismograph,[18] and a personal or bath scale.[19,20] In the majority of cases the natural frequency of the apparatus and the oscillations of the body itself have proved to be factors capable of affecting the appearance of the ballistocardiogram.[3,10,11,21-25]

A ballistocardiograph of new design, which records the ballistic thrusts of the body without the interferences encountered in other forms of the instrument has been described in a preliminary report.[20] The purpose of this article is to present a more detailed description of this ballistocardiograph and to show samples of records which may be obtained with it.

THE APPARATUS, METHODS OF USE, AND MATERIAL

Description of the Apparatus.—A diagram of the ballistocardiograph is given in Fig. 1. The platform is a plate of steel, $^1/_4$ inch in thickness and 14 inches square. This plate, *A*, is supported along one edge upon the rounded edge of a 1-inch angle iron, *B*. The opposite edge is supported only at its center by an angle iron, *C*, bolted to the plate at right angles to its edge. To prevent the plate from bending under the weight of the subject, it is reinforced beneath by a T-iron (not shown) which extends from one side to the other. The sharpened free margin of *C*, which may be called the force transmitter, rests upon the recording bar, *D*. The recording bar is a strip of steel, $1^1/_2$ inches in width and $^3/_{16}$ inch thick, supported at either end by the sharpened edge of a $^3/_8$-inch angle iron. The bar has a free length of $7^1/_2$ inches.

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Eight SR-4 strain gauges* are cemented to the recording bar along the line of contact with the transmitter. Below the bar, four gauges are cemented in a row across the line of force transmission, at right angles to the line. Above, where this arrangement is not feasible, the remaining four gauges are cemented in pairs at either side of the line.

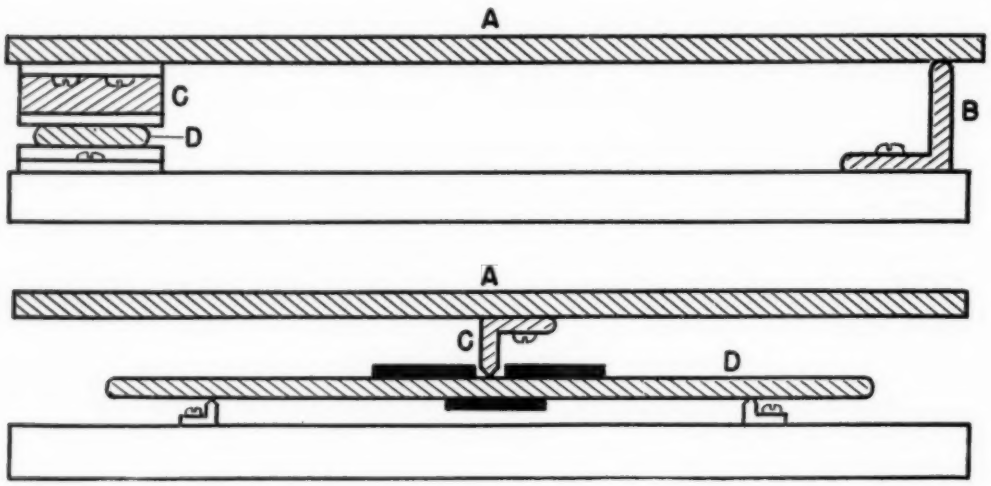

Fig. 1.—Side and front views of the electric strain gauge ballistocardiograph. *A*, steel plate, ¼ inch by 14 inches by 14 inches; *B*, 1-inch angle iron supporting one edge of the platform; *C*, angle iron with sharpened edge, bolted to the center of the opposite edge; *D*, steel recording bar, 3/16 inch by 1½ inches by 10 inches, supported on the sharpened edges of two small angle irons and having a free length of 7½ inches. Solid black strips on the recording bar indicate the positions of the strain gauges.

As shown in the circuit diagram (Fig. 2) the strain gauges are arranged as a Wheatstone bridge. Circulatory impacts of the subject's body are delivered via the transmitter to the recording bar. Deformations of the bar produce changes in length of the wire in the strain gauges. The electrical resistance is thereby altered and the bridge becomes unbalanced with each thrust. The magnitude of the voltage change varies in a linear fashion with the force of the impact. Some of the large waves in the ballistocardiogram of a normal subject represent voltage changes of the order of 0.2 millivolt. The placement of gauges both above and below the recording bar serves to increase the unbalance of the bridge since the two groups *X* and *Y* are deformed equally, but in opposite directions. The signal from the bridge is amplified and may be fed into either a cathode-ray oscillograph or an ink-writing oscillograph.

The over-all dimensions of the strain gauge ballistocardiograph in its carrying case are approximately 3 by 16 by 18 inches. The apparatus weighs 30 pounds including the 18-pound steel platform.

*The gauges are listed as Type C-5, each gauge having a resistance of 350 ohms. They are produced by the Baldwin Locomotive Works, Baldwin Southwark Division, Philadelphia, Pa.

Recording.—The subject stands upon the platform with heels together, one on either side of the position of the transmitter. The knees are fully extended, but are not locked forcibly. A backboard is provided, against which the subject rests his buttocks, shoulders, and head. Without a backboard, slight swaying movements of the body distort the record. Gentle contact of the body against the vertical backboard is sufficient to eliminate such movements and their effects upon the records. Ordinarily, it is unnecessary for the subject to hold his breath during the recording.

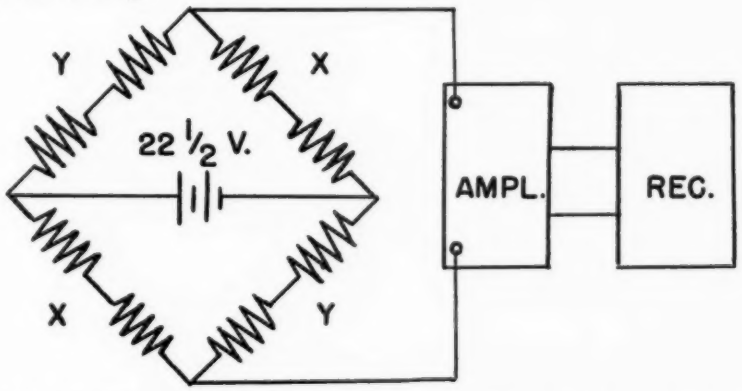

Fig. 2.—Circuit diagram of the ballistocardiograph. *X* gauges are placed above the recording bar, while *Y* gauges are placed beneath it. The signal resulting from an unbalancing of the bridge is amplified and recorded. The Offner ink-writing oscillograph was used in this instance.

All recording was done on the fourth floor of a brick building. Although the building is located beside a main thoroughfare carrying heavy traffic, no distortion of records by building vibrations was noted. It was unnecessary, therefore, to mount the ballistocardiograph upon rubber or other cushioning material.

The records presented in this paper were obtained with the Offner crystograph. An ink-writing oscillograph was preferred since it obviated the encumbrance and expense of photographic recording with a considerable saving of time. The operation of this ink-writer is based upon the phenomenon of the piezo-electric crystal which is deformed in direct proportion to the voltage applied to it. This further insures a deflection which is linear with the strain applied to the gauges. The number of oscillations per second in the ballistocardiogram (about fifteen) is well within the range of frequency which the oscillograph is able to record faithfully (1-100 cycles per second). The circuit diagram of the Offner amplifier is shown in Fig. 3.

The oscillograph was equipped with three channels, permitting the recording of respiration, electrocardiogram, and the ballistocardiogram simultaneously. The phases of respiration were recorded electrically by means of a copper-constantan thermocouple, installed in an ether cone. The active junction of the thermocouple, alternately warmed and cooled by the subject's respiration, produced the changes of potential. Electrocardiograms were taken using Lead I. While the electrocardiograms were slightly distorted in some cases, they nevertheless permitted a correlation of electrical and ballistic events in the cardiac cycle.

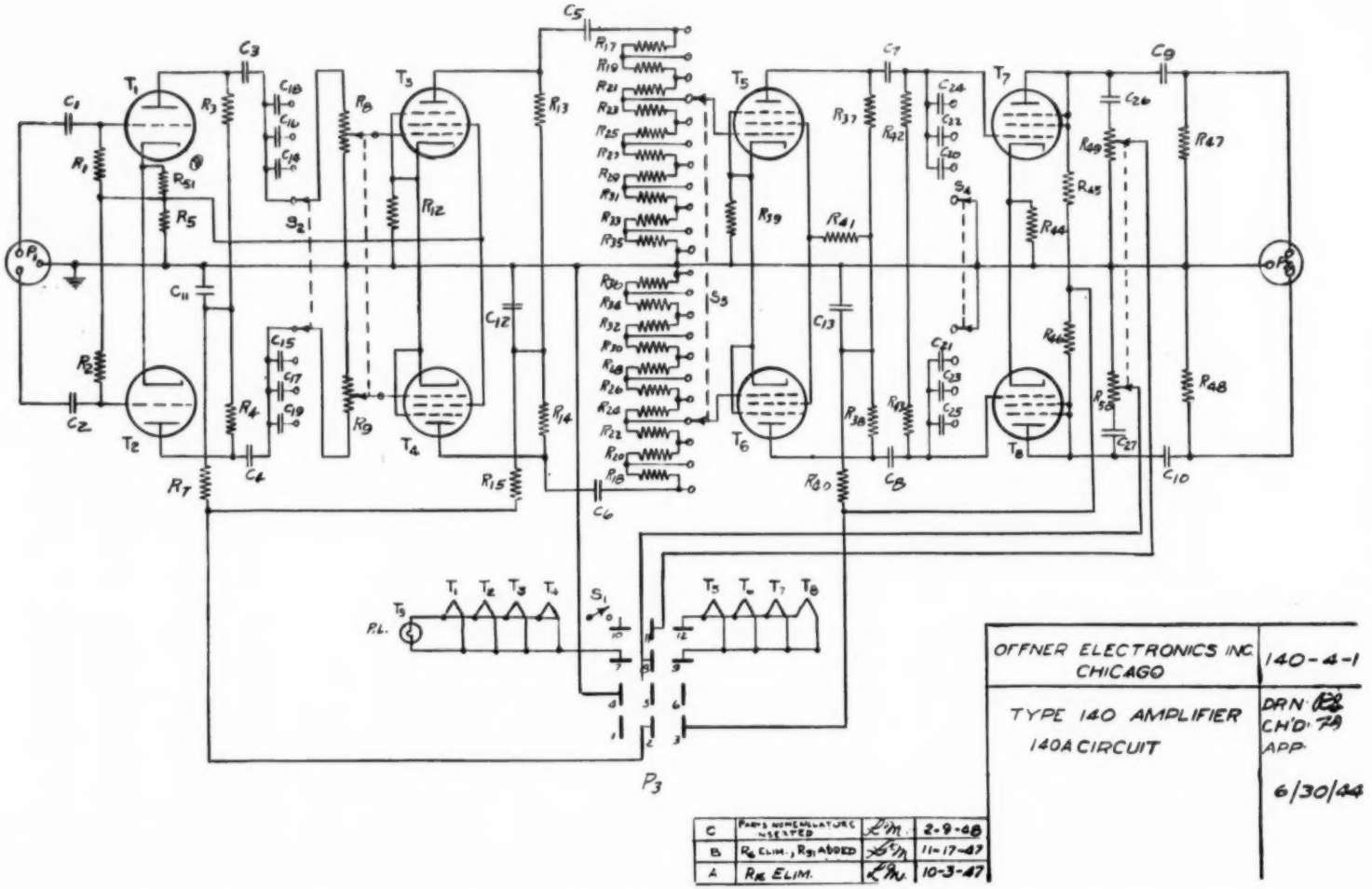

Fig. 3.—Circuit diagram of the Offner amplifier, type 140 (140A Circuit). (Permission to reproduce this diagram was kindly granted by Dr. F. F. Offner, Offner Electronics, Chicago, Ill.).

Subjects.—The ages of the subjects ranged from 15 to 65 years. However, the majority were young, healthy medical students and technicians with no known history of cardiac or circulatory disease.

NORMAL RECORDS

On the whole, the ballistocardiograms obtained with the electric strain gauge ballistocardiograph are similar in form to those published by other workers. The ballistic cycle begins with an upward deflection, H, followed by the large

Fig. 4.—Simultaneous records of respiration, ballistocardiogram, and electrocardiogram of subject E. G. The upper set of records was taken during quiet respiration; the lower, while the breath was held approximately midway between full inspiration and full expiration. The beginning of each respiratory phase is indicated by the symbol INSP. or EXP. The undulation of the ballistocardiogram's base line, related to the respiratory phases, disappears when the breath is held. Records are about one-third actual size.

IJK complex. The remaining waves are usually smaller and vary somewhat in amplitude and number with the subject. Their number is often decreased immediately after exercise.

The effect of respiration upon the ballistocardiogram, often noted by others—namely, an alternate increase and decrease in amplitude of the waves—was observed. In addition to this well-known feature of the ballistocardiogram, a second effect of respiratory activity impressed itself upon the records. There occurred a rhythmic undulation of the base line which was definitely correlated with the phases of respiration. This is illustrated in Fig. 4 (two sets of records of one subject). The upper record was taken during quiet breathing; the lower

was taken immediately afterward with the subject holding his breath. The respiratory irregularities obviously distort the record, but the base line becomes level when respiration is arrested. The records in Fig. 5 show the effect of exercise upon the appearance of the record. The upper record was taken during quiet

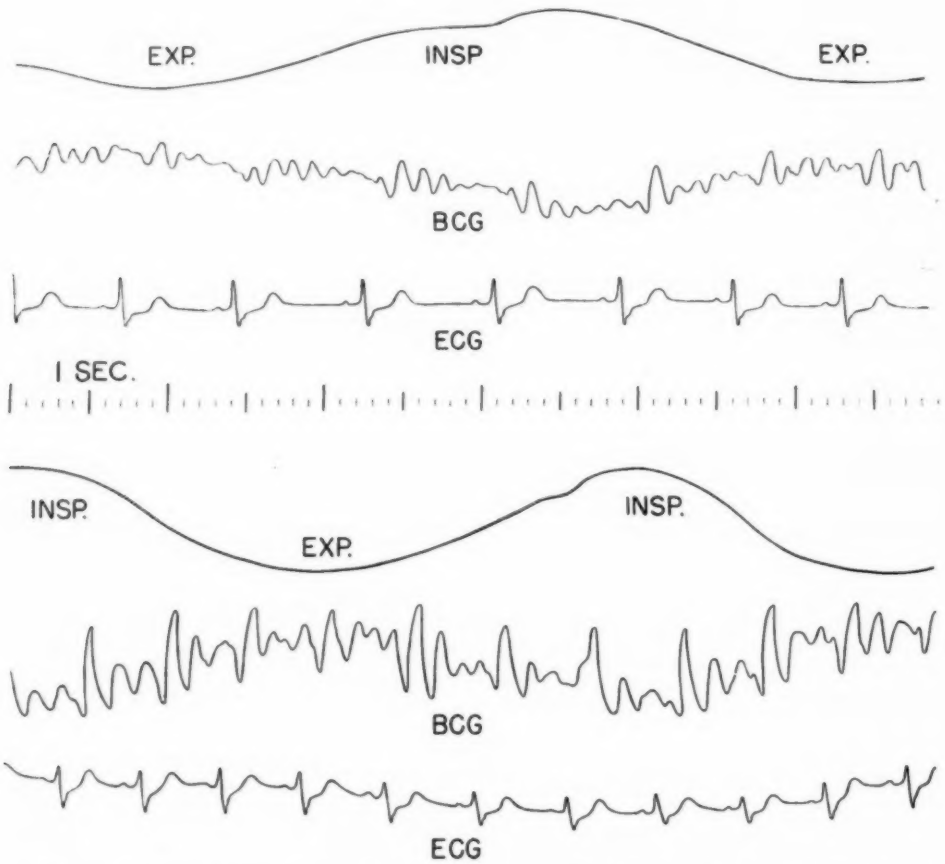

Fig. 5.—Records of subject E. G. before (upper set of records) and about forty seconds after (lower) mild exercise. Note the greater amplitude of the ballistic waves, especially H, I, and J, and the more pronounced undulation of the base line in the lower set of records. The beginning of each respiratory phase is indicated. Slightly less than one-half actual size.

breathing; the lower, immediately following mild exercise (squatting twenty-five times). In addition to the increased size of the waves, there is a more pronounced fluctuation of the base line. The latter is clearly associated with the deeper breathing of the subject. While, under certain conditions, respiratory activity disturbs the records, it is possible to obtain a level base line even during breathing by decreasing the capacity of the coupling condensers. The resulting attenuation of low frequencies eliminates the base-line undulation, and since this method was used in most experiments, it was unnecessary for the subject to hold his breath during recording.

A notable difference between the records here presented and those obtained with horizontal and some vertical ballistocardiographs is the constant occurrence of a small upward deflection between waves H and J[3] (Figs. 6, 7, and 8). In order to avoid confusion in subsequent references to this wave, it will be designated as I[2]. Starr and his associates[6,22,26] have pointed out that the beginning of the first upward deflection, H, of the ballistocardiogram occurs simultaneously with the beginning of the QRS complex of the electrocardiogram. This relationship readily

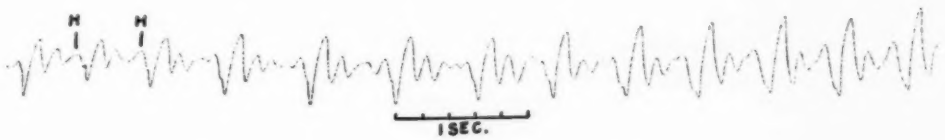

Fig. 6.—Record of subject V. K. The H wave is indicated in two cases. Wave I[2] immediately follows H and appears as a small upward deflection or shoulder upon the downstroke, HI. The record begins at complete expiration and ends at full inspiration. Note the migration of I[2] from a point between waves H and I down to I. Record is three-fourths actual size.

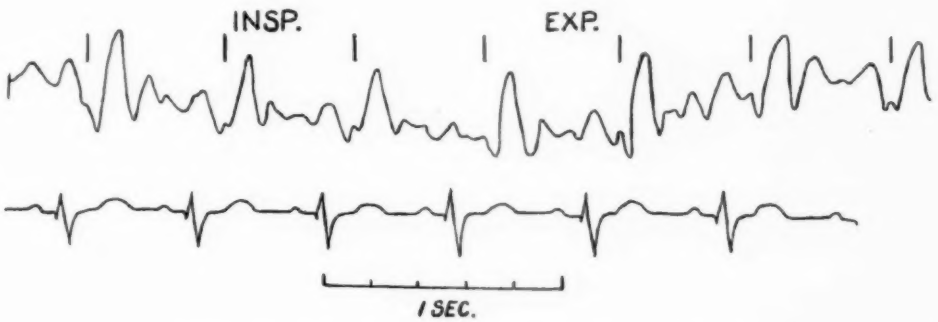

Fig. 7.—Simultaneous ballistocardiogram and electrocardiogram of subject V. K. The phases of the respiratory cycle are indicated. Vertical lines mark the positions of the I[2] waves. The drifting of I[2] is more pronounced here than in Fig. 6. I[2] oscillates from one side of the I wave to the other and in the last instance is located at the position of I. Record is two-thirds actual size.

identifies the H wave and aids in locating the position of I[2]. In Figs. 4, 5, and 7, showing simultaneous electrocardiogram and ballistocardiogram, H may be identified, and wave I[2] following it is clearly evident. The time interval between H and I[2] varies slightly from one cardiac cycle to the next so that I[2] may appear soon after H at some point on the downward stroke HI, on the ascending IJ stroke, or again as a distinct upward deflection at the position of I (Figs. 7 and 8,*A*).

Following exercise there occurs a great increase in the amplitude of the ballistic waves, particularly of I, J, and K (Figs. 5, and 8,*B* and *C*). As noted previously, the number of waves following the HIJ complex may be reduced just after exercise (Fig. 8,*B*). Immediately after mild exertion, I[2] is sometimes less distinct or even absent, but it usually begins to reappear after an interval of a few heart beats (Fig. 8,*C*).

DISCUSSION

While it should be possible to incorporate the strain gauge principle in a horizontal or bed-type ballistocardiograph, the vertical form of the instrument appears to offer a distinct advantage. With the subject in the horizontal position, a certain amount of the thrust or recoil is lost in moving the body about upon its

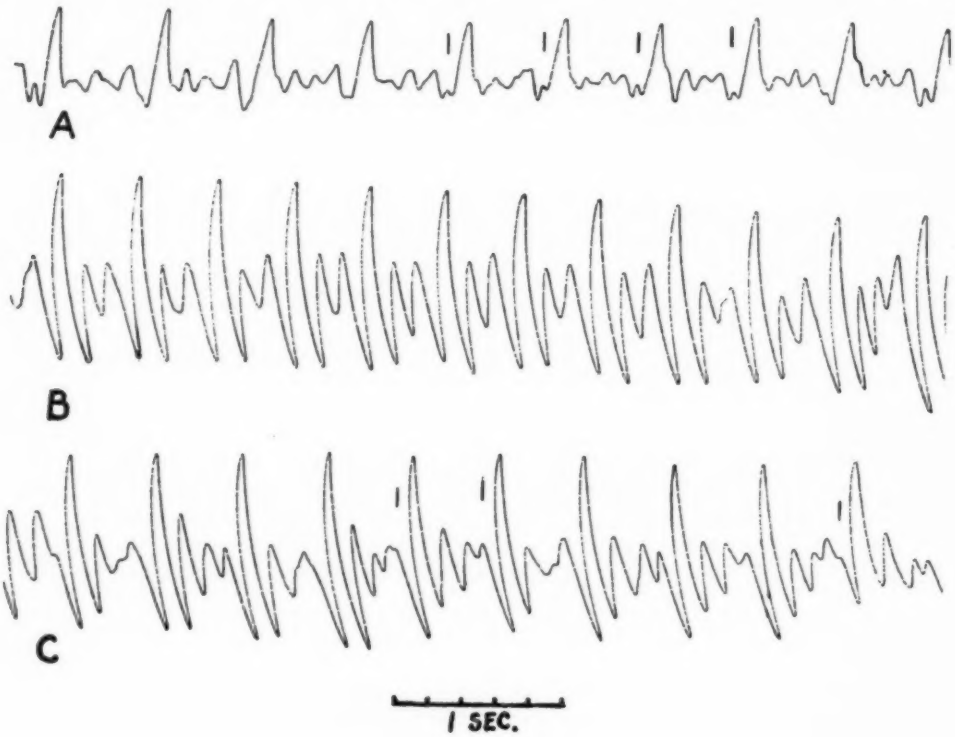

Fig. 8.—Records of subject J. B. The breath was held midway between inspiration and expiration. In record *A*, taken before exercise, the side-to-side migration of I^2, noted during breathing in Figs. 6 and 7 does not occur, but I^2 remains close to or at the position of the I wave. Vertical lines mark the positions of the I^2 waves. Record *B* was taken about sixteen seconds after mild exercise. Note reduced number of waves, the absence of wave I^2, and the pronounced increase in amplitude. Record *C* was taken about thirty-six seconds after exercise or about twenty seconds after the beginning of record *B*. The smaller waves of the ballistic pattern are already beginning to reappear. I^2 occurs occasionally and is indicated by the vertical lines. The heart rate is essentially the same in *B* and *C*, yet all of the small waves do not appear in *B*. (See discussion of this point in text.) Records are slightly smaller than actual size.

soft and elastic tissue supports. In vertical recording, however, the thrusts are delivered directly through the heels to the platform and recording bar. Consequently, a more complete transmission of the force obtains.

The vertical position is, of course, disadvantageous when it is desired to record ballistocardiograms on cardiac patients who are critically ill. However, if the patient is able to stand quietly for the duration of a few heart beats, satisfactory records are obtained.

The Natural Frequency.—It is of importance to know the natural frequency of any ballistocardiograph in order that its influence upon the shape of the ballistocardiogram may be taken into consideration. The frequency of the ballistocardiograph may be low[10,11,21] or high,[6,7,14] depending upon the design of the apparatus and the degree of damping provided. The bed type of ballistocardiograph, in general, is either suspended by wires, chains, or the like, or supported at the ends of strips of spring steel. The natural frequency of the apparatus is therefore determined by the lengths of the supports and by the weight of the bed; a problem of simple harmonic motion. In the case of the strain gauge ballistocardiograph, however, the mechanical situation is that of a simple beam having a force applied at its middle. The natural frequency of such a system is readily calculated. For the case in which the unloaded beam (recording bar) has a free length of 7½ inches and is struck a single blow, the calculated frequency is approximately 196 per second. The same beam, loaded with 150 pounds and struck a single blow should have a natural frequency of 13.6 per second. While the natural frequency of the apparatus may be determined upon theoretical grounds, it is difficult to find evidence of the influence of the frequency of the apparatus upon the form of the ballistocardiogram. Tests of the apparatus were conducted in which light blows or taps were delivered to the platform with and without a load equivalent to the weight of the living subject. Oscillographic records of these tests show an instantaneous deflection as the blow is delivered, and an immediate return to the base line without aftervibrations. It would appear from these observations that either the blows delivered were not of sufficient force to excite the natural frequency of the system, or that the vibrations which did occur as a result of the blow were of such small magnitude that the amplifier, when set at a gain suitable for recording the ballistocardiogram, did not render them evident.

Respiratory Variations.—The respiratory variation of the ballistocardiogram is frequently seen[6,22,26] and its cause is the subject of a recent paper.[27] It does not require discussion here. However, the undulation of the base line associated with the phases of the respiratory cycle deserves consideration. In the upper portion of Fig. 4 and in both parts of Fig. 5, records are shown in which the slow waves were permitted to appear (coupling condenser = 0.5 microfarad). The correlation of their direction with the phases of respiration is evident. This observation is best explained as the effect of diaphragmatic excursions upon the forces generated by the movements of the heart and blood. Upon inspiration, the downward thrust of the diaphragm tends to oppose headward circulatory forces, and to augment impacts directed toward the feet. The result is a downward shift of the base line of the record. The opposite occurs upon expiration; that is, the force of the diaphragm is added to headward impacts, while it opposes those of opposite direction. Consequently the base line is raised in expiration. In accord with this explanation is the observation that the base line becomes quite level when respiration is arrested. The lower record in Fig. 4 was made while the subject held his breath. The base line is level, although the amplifier circuit is set to permit the recording of waves of low frequency. As mentioned earlier, the attenuation of low frequencies makes it possible to record the ballistocardio-

gram upon a level base line during respiration. This feature represents a distinct advantage for it obviates several of the difficulties which are encountered with the low-frequency ballistocardiograph[10] which requires that the subject hold his breath during the recording (Starr[25], p. 197).

The Later Waves of the Ballistic Cycle.—The wave patterns in normal records obtained with the strain gauge ballistocardiograph are similar to those of other published records. However, they more closely resemble ballistocardiograms recorded by apparatus having a high natural frequency[6,7] than they resemble records of a low-frequency ballistocardiograph which have a number of the waves damped out.[10] Following H and the prominent IJK complex there regularly occurs a series of smaller waves. These waves vary in amplitude and are more prominent in some individuals than in others. Such waves have been reported by others, but have been variously interpreted as being merely aftervibrations due to tissue elasticity or as the records of real impacts (compare Nickerson and Curtis,[10] Hamilton and Dow,[15,28] and Starr and Wood[26]). Hamilton and co-workers[3] have pointed out that the later waves of the ballistocardiogram do not damp out readily, indicating that they represent a series of thrusts in the later parts of the cardiac cycle. In the cadaver, however, damping was quite rapid.[6] Furthermore, Hamilton has been able to correlate the later waves of the cycle with peripheral impacts of the blood and the periodic surging of blood in the aortic windkessel.[15,28] The presence of the diastolic waves in the author's records would appear to substantiate the statements of Hamilton and his co-workers[15,28] since the body stands, in this case, upon the platform and there is no opportunity for it to oscillate upon soft tissues. Nor can these waves be a result of aftervibrations of the apparatus, for tests show that if they are present, they are not recorded. Finally, the later waves in the cycle do not seem to be the records of oscillations of the viscous elastic mass of body tissue for there is no apparent correlation between the number and size of these later impacts and the body build of the subject.

Effect of Exercise Upon the Form of the Ballistocardiogram.—Following exercise there is a pronounced increase in amplitude of the waves of the ballistocardiogram. This is especially true of the larger waves which appear at the beginning of the cycle and is to be expected since these waves result from the ejection of blood from the heart, the thrust against the aortic arch, and similar events.

The disappearance of the I^2 wave after exercise has already been mentioned. I^2 returns after a short time, appearing at first occasionally, then regularly (Fig. 8).

The most significant observation to be made in records taken immediately following exercise is that the number of waves in the pattern of the ballistocardiogram is reduced. For example, in Fig. 8,*B*, taken about sixteen seconds after mild exertion, the later waves of the cycle (N and O) do not appear. This finding would, at first, appear to support one of the objections to the clinical use of the ballistocardiograph. Nickerson and Curtis[10] have pointed out that with high-frequency, undamped beds, an overlapping of patterns occurs with high

heart rates. In Fig. 8,*B* it appears that there had not been sufficient time for the recording of the last waves of the pattern and that the beginning of a new cycle had obliterated them. However, it will be observed in Fig. 8,*C*, a record taken about twenty seconds after that of Fig. 8,*B*, that the smaller waves have reappeared, although the heart rate is essentially the same as in the record which does not show them. With the recording system employed here, any thrusts delivered to the ballistocardiograph are recorded instantaneously and the number of waves which may be recorded in a cycle is limited only by the frequency response of the oscillograph (in this case, 100 cycles per second). Since this is so, one must conclude that the forces which are responsible for the production of the later waves of the pattern either do not occur just after exercise (when blood is being ejected with greatly increased force) or else they occur simultaneously for a time so that they appear as a single wave. A systematic search for an explanation of these observations has not been made, but the problem holds considerable interest and may be solved more readily when the forces expressed by each of the ballistic waves have been identified.

Significance of Wave I².—In a recent paper[29]* there is described a wave which is split off from the I wave. It appears in certain records and behaves somewhat like the wave which, in this article, has been termed I². In records obtained with the strain gauge ballistocardiograph, however, it appears consistently as a part of the pattern of the ballistocardiogram. While wave I² is located between the upward deflections H and J, its position with respect to these waves is not constant. I² may appear in an intermediate position at the point where I is usually seen. It may also occur earlier or later as a shoulder or a definite peak upon the downward slope of the H wave or the upward stroke of J. The shift in position of I² is not haphazard, but is a gradual one from side to side and is correlated with the phases of the respiratory cycle. Figure 7 shows a record in which this changing relationship is clearly demonstrated. In full expiration, I² is a headward deflection interrupting the downward slope, HI. As inspiration begins, it appears slightly later in subsequent cardiac cycles until, at the height of inspiration, I² appears upon the upward stroke, IJ. The distance along the time axis between a point near the peak of the H wave to one near the peak of J—the limits between which I² may occur—represents a period of approximately 80 milliseconds.

The identification of the event responsible for the production of I² is difficult, but invites speculation and a careful study of the ballistocardiographic records made simultaneously with those of respiration and the electrocardiogram.

The most useful clues to the cause of I² appear to be its location in the ballistic cycle and its correlation with respiration, mentioned above. The fact that I² may sometimes occur after the I wave (resulting from the ejection of blood by the heart), precludes the snap of the atrioventricular valves as a possible explanation.

***At the time of completion of this paper, no other description of a wave corresponding to I² had been seen by the writer. However, in a recent article Starr and Mayock[29] describe a "splitting or splintering" of the I wave. The wave which is split off from I appears and behaves somewhat like the one described by the writer. It seems likely that I² and the splintered I wave express the same type of circulatory impact, but do so in different ways because of a difference in the characteristics of the two types of recording equipment employed.**

Since I^2 appears slightly in advance of the stronger upward J wave (resulting from deceleration of the blood in its headward course and rounding the aortic arch) and has the same direction, the possibility is suggested that I^2 corresponds to a thrust against the pulmonary arch or against pulmonary resistance. The latter seems the more likely explanation inasmuch as there are respiratory waves in pulmonary arterial pressure associated with fluctuations of the intrathoracic pressure.[30] This idea is further strengthened by the observed correlation of the position of the wave with the phases of the respiratory cycle (Figs. 6, 7, and 8). In addition, Figs. 7 and 8 demonstrate that the shifting in the position of I^2 ceases with the arrest of respiration and that it becomes static between H and J. Further studies of the ballistocardiogram with simultaneous records of the electrocardiogram, pulse, and respiratory cycle should aid in the identification of I^2.

SUMMARY AND CONCLUSIONS

1. A vertical ballistocardiograph is described. The apparatus consists principally of a group of electric strain gauges arranged as a Wheatstone bridge. Circulatory impacts deform the gauges and unbalance the bridge, the signals of which are amplified and recorded.

2. The ballistocardiographic records of several normal subjects are presented and discussed. In certain cases simultaneous records of respiration and the electrocardiogram are given. In general, the records resemble those obtained with other forms of the instrument, both vertical and horizontal, but particularly those having a high natural frequency.

3. A notable feature of the records obtained with the electric strain gauge ballistocardiograph is a headward thrust which occurs between the upward deflections, H and J. This wave (I^2) migrates rhythmically between H and J in a manner which relates it to the respiratory cycle. It is suggested that I^2 may be the result of an impact in the pulmonary circuit.

4. The smaller waves which occur near the end of the ballistic cycle appear not to be mere aftervibrations, but rather the records of real circulatory impacts. These waves are reduced in number for a short while following exercise.

5. The electric strain gauge ballistocardiograph offers certain distinct advantages. The natural frequency of the apparatus apparently does not influence the form of the records. It is unnecessary for the subject to hold his breath while a record is being made. It is compact, portable, and inexpensive to construct.

The writer wishes to express his sincere thanks to Dr. Ernest D. Gardner of this department for his invaluable suggestions and assistance in this work. Doctors C. G. Johnston and E. S. Gurdjian of the Department of Surgery were most cooperative in rendering technical aid and making available their amplifying and recording equipment.

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BALLISTOCARDIOGRAPHIC PATTERNS IN INTRALUMINAL AORTIC OBSTRUCTIONS

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THE ballistocardiograph has been used extensively in the past ten years to determine cardiac output in various vascular conditions. During these studies it has become evident that abnormalities of the ballistocardiographic pattern consistently appear in the presence of certain pathologic states. This paper is concerned primarily with the abnormal pattern occurring in the presence of intraluminal aortic obstruction.

The phenomenon of body recoil following heart beat led a Scotsman, J. W. Gordon,[1] to build the first ballistocardiograph in 1877. In 1905, Henderson[2] described a ballistocardiograph which he had designed, and reported a study in which he had attempted to determine the movements of the circulation as reflected by the recoil curve. Other men made brief investigations in this field, but it was not until the early 1930's that continuous and effective study was begun.

In 1939, Starr and co-workers[3] published a description of a high-frequency ballistocardiograph, and since that time Starr has taken well over a thousand records in health and disease. He has emphasized the need for correlation of abnormal ballistocardiograms with disease entities.[4]

Nickerson and Curtis,[5] in 1944, described a low-frequency, critically damped ballistocardiograph, similar in principle to the machine designed by Henderson. In a subsequent study, Nickerson, Warren, and Brannon[6] demonstrated the reliability and clinical application of this instrument in determining cardiac output.

The records made by both the high- and low-frequency machines are similar and no great difference in results has been observed.[7]

THE CLINICAL STUDY

The abnormal patterns associated with two types of intraluminal aortic obstruction, coarctation of the aorta and insidious thrombosis of the terminal aorta, are described in this article. Eight patients with coarctation of the aorta and ten with thrombosis of the terminal aorta have been examined in the vascular clinic in the past twenty months. They have afforded an opportunity for extensive study of these two forms of aortic obstruction.

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The Ballistocardiograph.—The Nickerson modification of the ballistocardiograph was used in this study. It has a low, natural, undamped frequency of 1.5 cycles per second, and an incorporated critical damping mechanism. Only the deflections resulting from the initial impacts are recorded, the remainder, occurring subsequent to the systolic pulse wave, being damped out. This renders the Nickerson machine particularly suitable for the study of patients with thrombosis of the terminal aorta and coarctation of the aorta, since it is in these initial impacts that aberrations from the normal occur.

Method of Patient Study.—A complete medical history was taken on each patient. All examinations were carried out in a constant-temperature room. Instrumental examinations included blood pressure readings, oscillometry, skin temperature measurements, chest and extremity roentgenograms, angiograms, fluoroscopy, and plethysmography. Ballistocardiographic tracings were obtained at the time of the initial physical examination.

Diagnosis.—The clinical findings in coarctation of the aorta are well known and need not be reviewed here. In each instance the diagnosis of coarctation was confirmed by operation. The provisional diagnosis of insidious thrombosis of the terminal aorta was made on the basis of the following: a history of slowly progressive intermittent claudication in both lower extremities, aching pain in the hips following activity, coldness and pallor of both legs, and loss of the power of sustained erection; the physical findings of absent pulsations in the femoral arteries bilaterally, markedly diminished oscillometric readings and lowered skin temperatures over both legs and thighs, and the absence of aortic pulsations below the umbilicus. The provisional diagnosis was confirmed in each instance by operation or aortography. Leriche[8] and Elkin and Cooper[9] have recently reviewed the clinical features and treatment of insidious thrombosis of the terminal aorta.

Results.—Abnormal patterns were encountered in all of the eight patients with coarctation of the aorta, and in all of the ten patients with insidious thrombosis of the terminal aorta. Preoperative and postoperative tracings were made in all of the eight patients with coarctation, and in two of the ten patients with thrombosis of the terminal aorta. The type of operative treatment varied and is noted in each case. Sample tracings from three cases of thrombosis of the terminal aorta are shown in Fig. 1. Characteristic tracings showing the effects of operative treatment of coarctation are presented in Fig. 2. Normal records are presented for comparison.

DISCUSSION

There are three waves which are of particular significance in the Nickerson ballistocardiogram (Fig. 1,*A*). The first of these (I wave) is believed to originate from a footward recoil following the headward ejection of blood and footward movement of the heart. A greater headward deflection (J wave) then follows as the column of blood in the ascending aorta and pulmonary artery is first decelerated. A footward thrust or force follows, which is believed to be due to the impact of the column of blood in the descending aorta against the peripheral resistance, and is so timed that it drives the ballistic system footward across the base line, thus generating the K wave.[5,10]

An abnormality occurred in the K wave of the ballistocardiogram in all of the patients with intraluminal aortic obstruction which appeared to be characteristic in the presence of that lesion. It was consistently observed that this abnormal K wave did not approach the base line sharply, but tapered off irregularly, and that it was reduced in magnitude when compared with the normal K wave or was completely absent (Figs. 1 and 2).

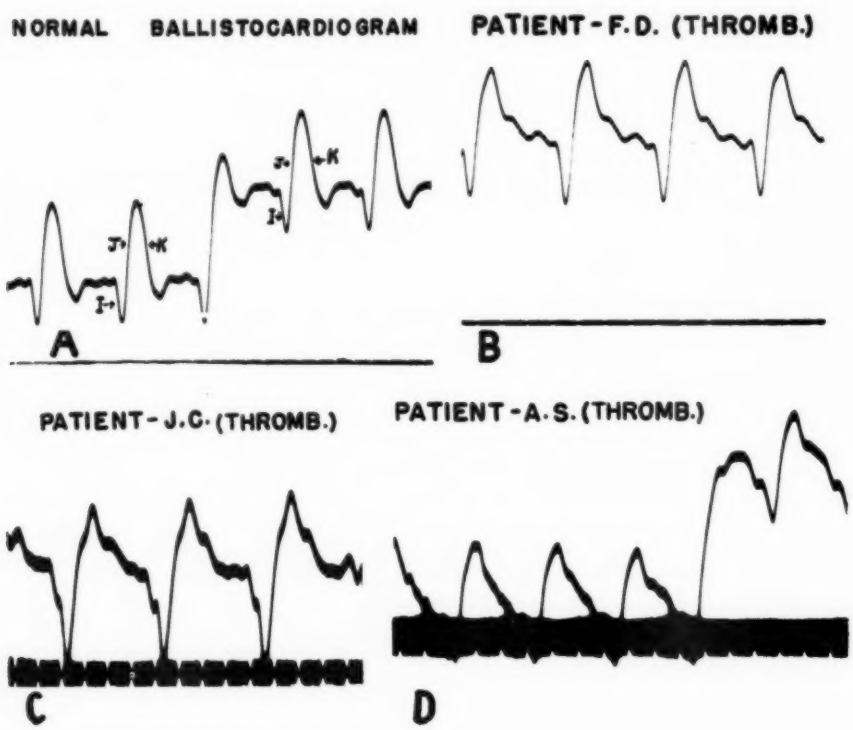

Fig. 1.—*A*, a normal ballistocardiogram. *B*, *C*, and *D*, characteristic tracings from three patients with thrombosis of the terminal aorta. Note the tapering, irregular K waves, as compared to the normal, and the consistency of this abnormality in the above tracings.

When the lumen of the aorta is narrowed or obliterated, the column of blood in the descending aorta meets a resistance earlier in its course and is diverted through branches and collateral channels proximal to the obstruction. Nickerson,[10] using an ingenious circulation model, has shown that variation in the length of the descending aorta is effective in changing the depth of the K wave. A complete absence of the K wave may also be produced, depending on the degree of constriction and the amount of shortening of the mechanical aorta. Hamilton and associates[11] were able to show, by synchronously recording the femoral pulse wave and the ballistocardiogram, that the peak of the femoral pulse contour was simultaneous with the deepest point of the K wave. These authors presented tracings from one case of coarctation and it was believed that the decreased K

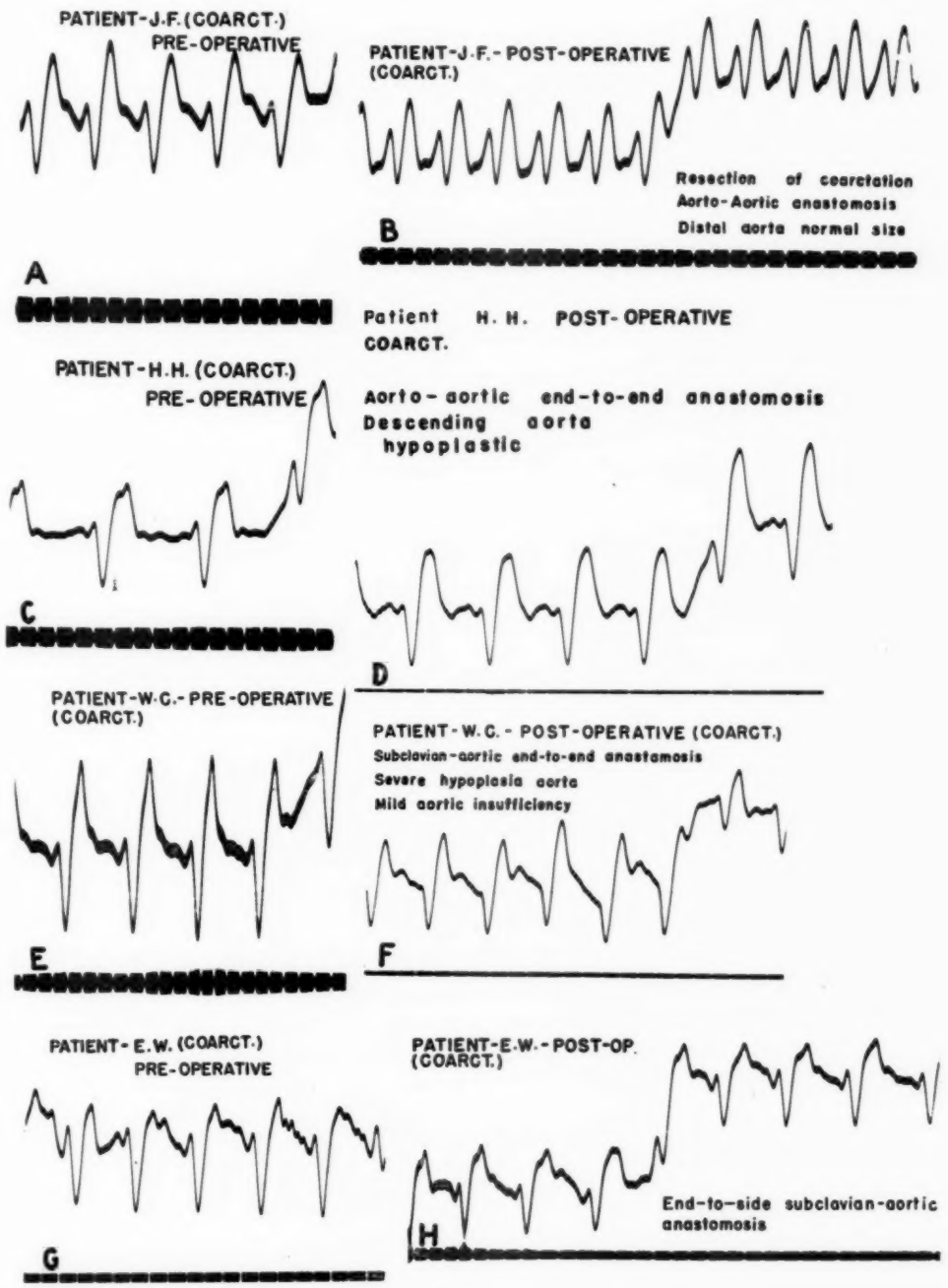

Fig. 2.—Characteristic tracings in coarctation of the aorta, showing the abnormal K waves and deep I waves. Note the effects of various operative procedures and the influence of the size of the distal aorta. Compare with normal K wave in Fig. 1,*A* and abnormal K waves in Fig. 1,*B,C,* and *D.*

wave seen was not a forced wave as was the normal K. The lack of standing waves and the lowered pulse pressure in the descending aorta below the coarctation were thought to be important factors in the production of the abnormal K wave.

Two additional factors which may be postulated in the explanation of the abnormal K wave are, first, the timing of the thrust produced by the blood meeting the abnormal obstruction and, second, the production of rebound forces at this time. It is believed that the footward thrust produced by the column of blood meeting an obstruction earlier than usual in its course is about equal in magnitude to that produced when the normal peripheral resistance is met. However, the net effect of this footward thrust is decreased because of its occurrence earlier in the cycle of events responsible for the I-J-K complex and because of rebound forces acting in a headward manner which are set up as the obstruction is met. Apparently, an important factor in the production of the normal K wave is the timing of the thrust, which is in turn dependent on the length of the descending aorta, in that its effect must not be dissipated before the ballistic system can be driven footward across the base line.

In four patients with coarctation it was noted that the I wave was increased in magnitude when compared with the I wave of a large series of normal ballistocardiograms. In three of these patients a concomitant increase in the J wave was observed, with the relationship or ratio of the I wave to the J wave being approximately equal to the normal. In two of the patients with absolute increases in the I and J waves the added factor of aortic insufficiency with increased stroke volume was probably responsible for the large I and J waves. Postoperative tracings from these two patients showed a return to more normal I and J waves with significant decreases occurring in the calculated stroke volumes. Postoperative tracings in the other two patients showed a return of I and J waves to normal size, and to a normal I-J relationship. Apparently stroke volume was not a factor in the production of the increased I and J waves of the two latter patients, in that the preoperative stroke volume was not significantly increased and no significant change in stroke volume followed operation although the I and J waves were decreased in magnitude postoperatively. A proved explanation of these findings cannot be given.

The character of the K wave and its degree of deviation from normal could not be correlated with certainty with the patient's symptomatology and physical findings. The abnormal K wave, however, was of definite aid in the diagnosis of either type of aortic obstruction presented here. This was true particularly in those patients not presenting typical symptomatology and physical findings.

An operative procedure designed to aid the circulation or to restore it to normal produced a variable effect on the tracing. In three patients having coarctation with resection and aorto-aortic anastomosis, the abnormal patterns returned to an almost normal form. This was true of the K wave only if the descending aorta was of normal size (Fig. 2,*A*). In one patient, with a normal distal aorta, in whom aorto-aortic anastomosis was performed, reversal of the abnormal K wave was not seen until the patient returned for the two months' postoperative examination. If hypoplasia of the descending aorta was present

(Fig. 2,*B*), aorto-aortic anastomosis did not alter the pattern markedly. Subclavian-aortic end-to-side anastomosis did not change the preoperative pattern (Fig. 2,*V*). Subclavian-aortic end-to-end anastomosis with a large subclavian artery produced a slight alteration of the pattern (Fig. 2,*C*). In two patients with thrombosis of the terminal aorta, bilateral lumbar sympathectomy did not alter the abnormal K wave.

It would appear that the ballistocardiogram continues to mirror alterations in the internal caliber and patency of the aorta and in the downward course of the pulse wave even though operative treatment has altered the over-all vascular physiologic process.

In his study of ballistocardiographic tracings, Starr[7] has been concerned chiefly with the pattern seen in myocardial dysfunction, and has not discussed or shown the abnormalities found in aortic obstruction. Hamilton, Dow, and Remington,[11] in discussing the relationship between cardiac ejection waves and ballistocardiographic forces, made the earliest mention of those involved in coarctation of the aorta, and presented tracings from one patient. A short J-K downstroke was noted. Brown and his co-workers,[12,13] using the Starr (high-frequency) type of ballistocardiograph have noted shallow, irregular K waves in six patients with coarctation. They call particular attention to the ballistocardiogram as a diagnostic aid for these patients. Reversal of the abnormal form followed operative treatment in one of the patients. Nickerson has reported a study of abnormal patterns, including coarctation of the aorta, with particular emphasis being placed upon the significance of the H and K waves. His clinical study of the K wave included one patient with coarctation for whom preoperative and postoperative tracings were made. Only slight change in the K wave followed operative treatment. No mention was made of the size of the descending aorta.[10]

Ballistocardiographic studies in thrombosis of the terminal aorta have not been reported in the literature.

SUMMARY AND CONCLUSIONS

The ballistocardiograph has been used chiefly to determine cardiac output. A second potentiality, however, lies in its use for determining aberrations of the heart and vascular system.

Characteristic ballistocardiographic tracings selected from ten patients with thrombosis of the terminal aorta and eight patients with coarctation of the aorta are presented.

The consistently abnormal pattern found in intraluminal aortic obstruction is discussed in detail and also in regard to its aid in diagnosis and its appearance following operative procedures.

It was concluded that the ballistocardiogram is of definite aid in the diagnosis of intraluminal aortic obstruction, especially in patients not presenting the typical findings. It may be used, limitedly, in evaluating the results of operative treatment, especially in coarctation of the aorta. The value of the ballistocardiogram in long-term, follow-up studies of operative treatment for aortic obstruction has not yet been determined.

The author wishes to express his appreciation to Dr. John L. Nickerson, of the Department of Physiology, Columbia University, for initial impetus and stimulation in this study. Dr. Nickerson built the ballistocardiograph used here.

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ALTERATIONS IN THE CIRCULATION DURING CARDIAC TAMPONADE DUE TO PERICARDIAL EFFUSION

An Experimental Study Employing Cardiac Catheterization

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TWO diseases of the pericardium have similar effects on the circulation. These are pericardial effusion with cardiac tamponade and constrictive pericarditis. Burwell and Blalock[1] and Lyons and Burwell[2] have defined the pathologic physiology of constrictive pericarditis. Cohnheim[3] and Starling[4] first demonstrated the effects on the circulation of injecting fluid into the pericardial sac. It is our purpose to extend the studies of these latter authors and to show experimentally certain of the similarities in the circulatory dynamics of these two disorders. In addition, our observations suggest a means of recognizing the presence of pericardial effusion in instances where this diagnosis is difficult to establish by the usual methods of examination.

METHODS

Nine dogs varying in weight from 7.0 to 24.0 kilograms were employed. The anesthesia used was intravenous sodium pentobarbital, 32 mg. per kilogram of body weight. Through a transthoracic approach, a ureteral-type catheter was sutured into the pericardium on its anterior surface, inferiorly and to the left, just above the apex of the heart. The catheter was led out through the chest wall where it was attached to a T tube, one arm of which was connected to a saline manometer; the other, to an adapter fitted for the injection of fluid. The thoracic cavity was emptied of the admitted air by distending the lungs with the positive pressure respirator. Ample time was allowed for restoration of normal conditions before observations were undertaken. For determination of the venous and arterial pressures, cannulae were inserted into the femoral vessels and connected to a saline and mercury manometer, respectively. To obtain the intracardiac pressures a No. 8 F radiopaque catheter was introduced in accordance with the method of Cournand and Ranges.[5] The levels were recorded by means of the Hamilton,[6] or a saline, manometer. Heparin, 0.5 to 1.0 mg. per kilogram of body weight, was administered to minimize clotting of the blood. The point of reference of all manometers was arbitrarily set at the top of the restraint board, 90.0 cm. from the floor. As confirmed by autopsy examination this level was found to be dorsal to the anatomic location of the right auricle by from 4.0

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*This work was done during the tenure of a Life Insurance Medical Research Fellowship.

to 8.0 centimeters. As we were interested primarily in the changes in pressure in a given animal no effort was made to correct the observed pressure to the true reference point.

The animal was placed in the recumbent position on a restraint board and was maintained under light anesthesia by means of the sodium pentobarbital. After the pressures, pulse, and respirations had reached a stable state, normal saline solution was injected into the pericardial sac in 10- to 50-ml. volumes.

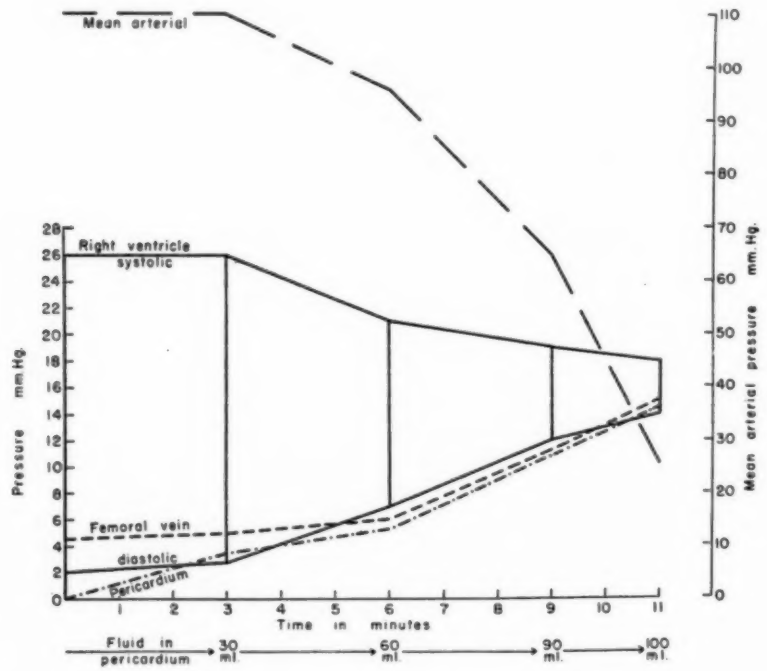

Fig. 1.—Typical circulatory changes produced by injecting fluid into the pericardium (Experiment No. 13, *b*).

Following a suitable interval, usually two to four minutes, the pulse and respiratory rates and manometer readings were recorded simultaneously.

The following additional data were obtained in certain of the experiments. The abdomen was opened through a right upper quadrant paramedian incision. A length of polyethylene plastic tubing was inserted into one of the primary tributaries of the portal system and fed into the portal vein to a position just beneath the lower border of the liver. The tubing was led out through the abdominal wall and connected to a saline manometer. Normal saline solution was allowed to run into the vein at a rate of approximately 1.0 to 2.0 ml. per minute to insure patency of the system. The abdominal wall was tightly closed by careful approximation and suture of all layers. Pressures were recorded at the same time as those from the other manometers.

The location of the intracardiac catheter was confirmed by fluoroscopy during the procedure. Each animal was examined post mortem to observe the integrity and exact location of the pericardial and portal cannulae and to insure the absence of any source of leakage.

OBSERVATIONS

As the basis for this report, data were collected on the effects of injecting fluid into the pericardium in eleven experiments on nine dogs. As shown in Fig. 1, the introduction of saline solution into the pericardium was followed by

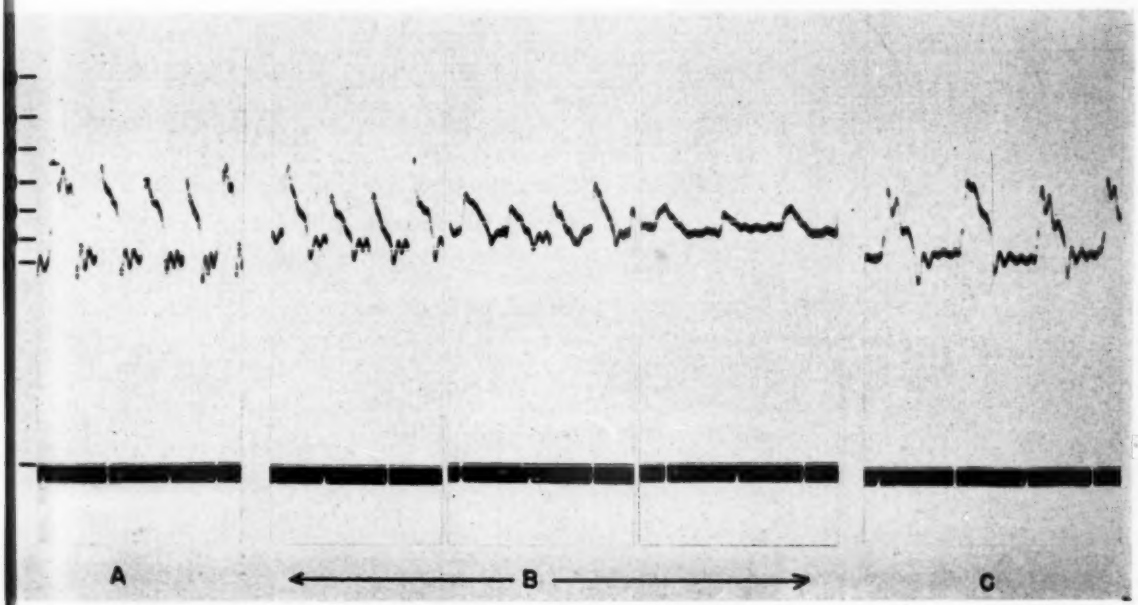

Fig. 2.—Pulse pressure contours in right ventricle as tamponade develops. *A* is the control period; *B* represents the presence of 60, 90, and then 100 ml. of fluid within the pericardium; *C* is the recovery period immediately after removal of the fluid.

a progressive elevation of the average diastolic pressure* in the right ventricle. The intraventricular tension increased equally and in direct relationship with that induced within the pericardium. The behavior of the average systolic pressure* in the right ventricle was not as consistent. The pressure fell and the decline was slower to appear and usually less abrupt than the rise in diastolic pressure. In one instance, Dog No. 14, there was no reduction of the systolic level although the pulse pressure was narrowed. The range of increase in the diastolic level was 9 to 14 mm. Hg; the range of decrease in the systolic level was 0 to 16 mm. of mercury. These changes resulted in an extremely narrow pulse pressure in the ventricle at the time of maximal cardiac tamponade (Fig. 2). This time was considered to be that period of the experiment in which the mean arterial pressure dropped precipitously. It was characterized by severe deterioration in

*These values represent the arithmetical average of the pressures recorded in inspiration and expiration during several respiratory cycles.

the animal's condition, including rapid shallow breathing and often cyanosis of the tongue. The heart rate was a less reliable sign in view of the variations in rate that accompany barbiturate anesthesia.

The pressure in the femoral vein was observed to rise slowly until it was approached by the pericardial pressure, when it increased more briskly and continued at a level essentially the same as that within the pericardium. The height of the venous column at the period of maximal tamponade represented a one- to three-fold increase over the original level. The volume of fluid required to achieve the peak effect varied greatly. It was noted that the pericardium rapidly adapted itself to a given volume of fluid in that repeat observations in the same animal required a larger volume to achieve the same degree of tamponade. The range of increase was from 10 to 25 per cent. A summary of the data at the period of maximal tamponade is included in Table I.

TABLE I. SUMMARY OF DATA AT THE PERIOD OF MAXIMAL CARDIAC TAMPONADE

DOG NUMBER	SEX	WT. (KG.)	PERICARDIAL FLUID (ML.)	PERICARDIAL PRESSURE*	RIGHT VENTRICULAR PRESSURE†			FEMORAL VEIN PRESSURE*	MEAN ARTERIAL PRESSURE
					SYSTOLIC	DIASTOLIC	PULSE PRESSURE		
4	M	14.2	80	24	—	—	—	23	50
6	F	12.0	90	20	—	—	—	21	20
7	F	7.2	100	13	—	—	—	13	20
8	M	15.0	80	14	—	—	—	14	40
10, *a*	M	21.0	150	14	20	14	6	14	40
10, *b*	M	21.0	165	15	—	—	—	12	10
11	F	17.8	110	17	26	17	9	15	60
12	F	24.0	160	12	19	14	5	14	45
13, *a*	M	7.0	80	13	19	13	6	13	25
13, *b*	M	7.0	100	14	18	14	4	14	25
14	M	21.0	180	17	31	20	11	17	60

All pressures are recorded in millimeters of mercury.
*Pressures measured with a saline manometer and converted to mm. Hg.
†The systolic and diastolic pressures represent the average of the respective pressures recorded in inspiration and expiration during several respiratory cycles.

Pressures were recorded in the portal vein in three experiments. These were found to be higher initially than the comparable femoral venous levels by from 40 to 80 mm. of saline. As the pericardial effusion was induced the portal pressure remained consistently higher than the femoral pressure until severe tamponade supervened. At this point the pressures within the pericardium, portal system, and femoral vein were approximately equal. These relationships are shown in Fig. 3.

DISCUSSION

It is apparent from examination of Table I that the alterations in the circulation are related to the pressure exerted within the pericardium and not to the volume of fluid therein. This is consistent with findings in patients in whom

the rate of development of the fluid in the pericardial sac is one of the primary factors in the production of cardiac tamponade. In tuberculous pericarditis, effusions up to 1,000 to 1,500 ml. have been described at autopsy where bedside examination revealed no evidence of cardiocirculatory embarrassment. And conversely, in patients with fluid appearing suddenly, as in those with stab wounds of the heart or acute fibrinous pericarditis, volumes of only 200 ml. have been found at autopsy in patients with advanced signs and symptoms of cardiac tamponade.

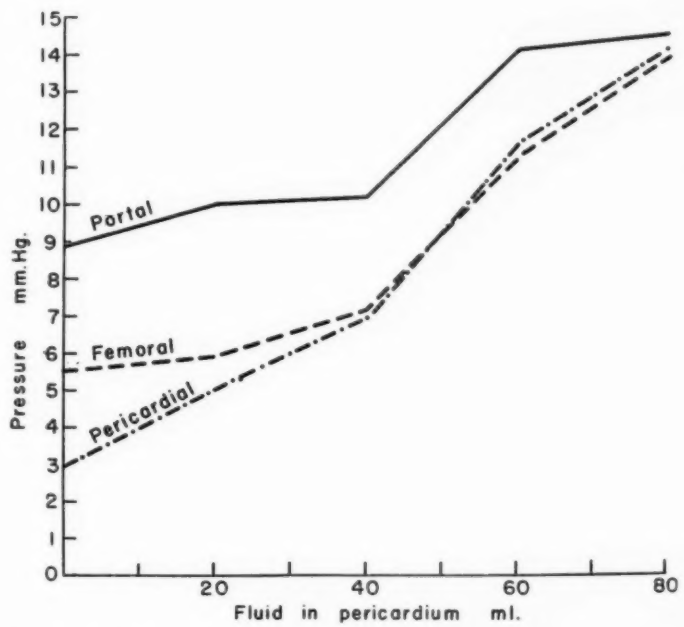

Fig. 3.—Pressures in the portal vein, femoral vein and pericardium as tamponade is produced.

The following sequence of events in the hemodynamics of acute pericardial effusion is suggested by these experiments. As the mechanical compression of the heart increases, the mean diastolic tension in the ventricle rises and is accompanied by elevation of the mean auricular pressure. The peripheral venous pressure then comes under the influence of the elevated auricular pressure. At a critical level of intrapericardial tension the hydrostatic force within the great veins is no longer adequate to dilate and fill the auricle. With the development of inflow stasis the cardiac output decreases and the mean arterial blood pressure falls. Since numerous authors[3,4,7] have shown that the peripheral resistance is maintained in pericardial tamponade, it can be stated that the fall observed in the mean arterial pressure is an expression of decreased stroke volume.

The alterations in the circulation in constrictive pericarditis, as discussed by Burwell and Blalock[1] and Lyons and Burwell[2], are elevation of the peripheral venous pressure, diminished output of the heart, and low peripheral arterial

pressure. All of these findings are observed to develop in the animals with experimentally induced pericardial effusion as has been pointed out.

A consistent feature in all experiments is the narrow pulse pressure in the right ventricle. The contraction of the normal range between the systolic and diastolic pressure arises from the elevation of the latter without proportionate increase in the former. In fact in all but one of the experiments the systolic level is seen to decline. As stated by Bloomfield and associates,[4] this pressure relationship may suggest or confirm the presence of constrictive pericarditis. In the example they report they observed an elevated mean diastolic pressure, a virtually normal systolic pressure, and a narrow pulse pressure in the right ventricle. Studies by Dexter and associates[9] have confirmed the presence of the contracted pulse pressure in the right ventricle in two proved instances of constrictive pericarditis and in two additional instances in which the diagnosis was well established by other means. In other forms of passive congestion due to failure of the heart, catheterization of the right ventricle usually reveals elevation of the systolic as well as diastolic pressure with either a normal or increased pulse pressure. Theoretical considerations suggest that an elevated diastolic pressure without proportionately elevated systolic pressure might be found in mitral stenosis or other states of cardiac decompensation involving preponderantly the right ventricle. In any event it is reasonable to predict that the contracted pulse pressure will be observed uniformly in advanced cardiac tamponade due to constrictive pericarditis or pericardial effusion.

The use of intracardiac catheterization in recognizing pericardial effusion in man deserves consideration. The narrow pulse pressure should be found in any instance in which the fluid is causing substantial cardiac compression. The application of this technique might be of value for those patients in whom the usual diagnostic measures are unable to differentiate pericardial effusion from severe cardiac dilatation or hypertrophy. This is particularly true since the risk of the method is less than that of the exploratory pericardial tap. McMichael[10] and Cournand[11] report an absence of serious complications in their extensive experience with the catheterization procedure.

The data on portal vein pressure are noteworthy for the evidence that the portal pressure maintains its elevated level, in relation to the peripheral venous pressure, until late in the accumulation of pericardial fluid. Williamson[12] has shown that fluid in the pericardium first collects along the lower margin of the heart, particularly along its diaphragmatic surface. This location of the fluid would favor early interference with inflow from the hepatic veins and inferior vena cava, and possibly explain the disproportionate enlargement of the liver and edema of the lower extremities seen in some patients. Although the portal pressures in our data do not bear out Williamson's concept, it is possible that the recorded values pertain only to acute experiments such as these. Our observations tend to support the concept of an hepatic sphincter, an alternative explanation. Arey and Simonds[13] have shown that the hepatic veins of the dog exhibit a relative increase in the thickness of the muscle layer. On this basis the theory has been advanced that the hapatic veins may dilate or contract in partially regulating flow in the portal system. The existence of this histologic feature has not been demonstrated in the hepatic vein of man.

SUMMARY AND CONCLUSIONS

1. An experimental method for evaluation of the hemodynamic changes in pericardial effusion has been described in detail.

2. Studies of the alterations of the circulation in pericardial effusion were completed in eleven experiments in nine dogs. With cardiac tamponade, a narrow pulse pressure was found in the right ventricle in the six instances in which the pressure was recorded by the optical manometer. The contracted pulse pressure is the result of elevation of the diastolic pressure without corresponding increase in the systolic pressure.

3. It is suggested that the detection of this pressure relationship by catheterization of the right side of the heart may aid in the recognition of pericardial effusion as well as constrictive pericarditis.

4. The higher pressure in the portal vein in relation to the peripheral venous pressure is maintained until the tamponade effect is at or near its height.

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RENAL HEMODYNAMICS IN HEART DISEASE

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DISTURBANCES of renal function have long been known to exist in the presence of congestive heart failure.[1,2] In 1944 Warren and Stead[3] suggested that cardiac edema was secondary to retention of salt and water by the kidneys. These authors attributed the disturbances in renal function to a decreased cardiac output rather than to engorgement and passive congestion secondary to increased venous pressure. They further postulated that the disturbance might be more directly related to decreased renal blood flow. Merrill[4] in 1946 and more recently Mokotoff and associates[5] have clearly demonstrated a marked decrease in renal plasma flow and rate of glomerular filtration in congestive heart failure. It became of further interest, however, to determine whether these changes could be correlated with various phases of heart disease. Furthermore, no previous studies of tubular function, utilizing the maximal tubular excretory capacity for para-aminohippurate, have been reported in patients with organic heart disease. Thus it was decided to include a study of this function as a part of our investigations.

METHODS

Renal studies utilizing the clearance and saturation methods, devised by Smith, Goldring, Chasis, and co-workers,[6-9] were conducted on twenty-six male patients with nonhypertensive organic heart diseases. Hypertensive patients were excluded since it was felt that renal vascular changes might be present out of proportion to the degree of cardiac involvement. Similar renal studies were conducted on eight normal men who were clinically free of cardiovascular and renal diseases. The small control series was established primarily as a check on the methods employed by this laboratory since adequate normal values have been established on larger groups by other investigators.[6-8] The effective renal plasma flow and the maximal tubular excretory capacity were measured by the use of sodium para-aminohippurate, and the glomerular filtration rate was measured by the clearance of mannitol. Merrill[4] has shown that the clearance of para-aminohippurate is a valid measure of the renal plasma flow in patients with congestive heart failure.

All patients were prepared for study in the usually accepted manner.[4,8] For the study of the effective renal plasma flow and the glomerular filtration rate a priming infusion consisting of 2.0 to 5.0 ml. of 20 per cent sodium para-amino-

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hippurate solution and 75 ml. of 25 per cent mannitol solution was administered. In order to obviate the need for a large volume of a sustaining infusion a constant injector was devised which delivered a calculated volume of 0.996 ml. per minute from a 100-ml. syringe. The sustaining infusion consisted of 4.0 to 10 ml. of the sodium para-aminohippurate solution, 75 ml. of the mannitol solution, and sufficient normal saline solution to make the total volume up to 100 milliliters. The priming and sustaining doses of sodium para-aminohippurate were estimated for each patient in an effort to obtain a blood level of approximately 2.0 mg. per cent. After an equilibration period of forty-five minutes the bladder was emptied through a multi-eyed indwelling rubber catheter, washed with 20 ml. of saline solution, and finally cleared with air and pressure. Multiple urine collection periods were used and a blood sample was drawn at the mid-point of each period. The blood pressure and pulse were measured and recorded once during each period.

When the maximal tubular excretory capacity was to be measured, the constant injector was temporarily discontinued. A priming infusion of 80 ml. of sodium para-aminohippurate was administered through the needle and tubing at the rate of 5.0 ml. per minute. The sustaining infusion consisted of the undiluted stock solution of sodium para-aminohippurate delivered from the 100-ml. syringe at the rate of approximately 1.0 ml. per minute. After an equilibration period of thirty minutes the bladder was again emptied as before and urine from three fifteen-minute collection periods obtained. Blood samples were drawn at the mid-point of each period.

Early in our studies on the maximal tubular excretory capacity considerable difficulty was encountered in obtaining adequate tubular saturation as measured by the $\frac{\text{load}}{T_{pah}}$ ratio. This difficulty arose only in those patients with a marked reduction in the renal plasma flow as occurred during chronic congestive failure. Since the load is the product of the plasma para-aminohippurate concentration and the difference between the effective renal plasma flow and the glomerular filtration rate,

$$L = P_{pah}\ (R.P.F. - G.F. \times 0.83),$$

a marked decrease in the renal plasma flow necessitated high concentrations of plasma para-aminohippurate. Initial experience proved that priming and sustaining doses less than the amounts given above failed to produce blood concentrations adequate for tubular saturation. The minimal plasma concentration of 60 mg. per cent recommended by Goldring and Chasis[6] was inadequate for the measurement of the maximal tubular excretory capacity in many cases of congestive heart failure. Smith[7] has advocated a $\frac{\text{load}}{T_{pah}}$ ratio greater than 2.0 for saturation of all nephrons; however, from the titration curves presented by this author it is apparent that a ratio greater than 1.5 results in saturation of more than 95 per cent of the tubules. Goldring and Chasis[6] consider a $\frac{\text{load}}{T_{pah}}$ ratio of 1.5 or greater as satisfactory evidence for tubular saturation.

Para-aminohippurate and mannitol were determined in cadmium filtrates of plasma and in diluted urine samples using the methods described by Smith, Goldring, and Chasis.[6,9] The renal plasma flow, the glomerular filtration rate, and the maximal tubular excretory capacity were calculated according to the methods of Smith.[7]

Measurements of vital capacity, venous pressure, and circulation time were obtained on the subjects on the same day that the renal function studies were carried out. The venous pressure was measured by means of a saline-filled glass manometer connected to the antecubital vein with the zero point of reference taken as 5.0 cm. below the fourth costochondral junction. The circulation time was determined in most instances by the use of a 2.0 per cent solution of sodium cyanide (0.11 mg. per kilogram of body weight). In some cases an arm-to-tongue circulation time was determined by the use of calcium gluconate or Decholin.

RESULTS

In each instance the recorded figures for effective renal plasma flow, glomerular filtration rate, and maximal tubular excretory capacity represent the average for at least two, and usually three, determinations. In order to make the data comparable and consistent with currently reported data all results were corrected to a body surface area of 1.73 square meters. In all cases the normal weight of the patient was used in the determination of the surface area. For the purpose of this study the patients with organic heart disease were divided into three groups. Group A (Table II) consisted of five patients with rheumatic valvular heart disease but without previous or present evidence of congestive heart failure. Group B (Table III) consisted of twelve patients with congestive heart failure at the time of admission to the hospital. However, these patients were edema free and clinically compensated at the time of determination of the renal hemodynamics. Clinical compensation was achieved by digitalization, bed rest, and a salt-free diet. Group C (Table IV) consisted of thirteen patients in whom cardiac decompensation was present at the time of study. Nine of these patients had peripheral edema varying from a trace to four plus; the other four had pulmonary congestion and hepatomegaly. Four patients (P.R., D.S., T.G., and H.H.) were studied both during decompensation and at a time when they were clinically compensated and are therefore included in both Groups B and C.

Effective Renal Plasma Flow (R.P.F.).—The mean R.P.F. in eight male patients without clinical evidence of cardiovascular or renal disease was 603 ±84.4 ml. per minute (Table I). This is comparable to the normal clearance of para-aminohippurate reported by other investigators.[4,9] The mean R.P.F. in patients with rheumatic valvular heart disease without previous or present evidence of congestive heart failure (Group A) was 433 ± 97.2 ml. per minute (Table II). As compared to the normals this represents a statistically significant decrease in the mean effective renal plasma flow (P. less than 0.01). In the patients admitted with congestive failure but edema free and clinically compensated at the time of study (Group B) the mean R.P.F. was 320 ± 86.5 ml. per minute (Table III). Comparing this Group with Group A there is also a significant

difference in the mean R.P.F. (P. less than 0.05 but greater than 0.02). In those patients studied at a time when they were decompensated (Group C) the mean R.P.F. was 190 ± 58.2 ml. per minute (Table IV). This value is almost identical to that given by Mokotoff and his associates[5] for patients with congestive heart failure and edema (191 ± 54.4). The difference in the mean effective renal plasma flow between Group C and Group B is highly significant (P. less than 0.01).

TABLE I. CONTROL GROUP. RENAL STUDIES IN PATIENTS WITHOUT CARDIOVASCULAR OR RENAL DISEASE

PATIENT	AGE	R. P. F.	G. F.	F. F.	$T_{M_{pah}}$
		ML. PER MIN. PER 1.73 SQ. M.		PER CENT	MG. PER MIN. PER 1.73 SQ. M.
R. C.	20	725	111	15.3	——
L. B.	45	697	110	15.7	60.8
R. O.	21	551	113	20.5	99.4
A. K.	33	651	99	15.2	54.5
G. P.	29	490	103	21.0	71.3
D. V.	24	512	92	18.0	97.1
M. N.	30	593	102	17.2	73.4
G. L.	30	601	97	16.1	105.7
Mean		603	103	17.4	80.3
Standard deviation		84.4	7.4	2.3	20.3

R.P.F. = effective renal plasma flow; F.F. = filtration fraction; G.F. = glomerular filtration rate; $T_{M_{pah}}$ = maximal tubular excretory capacity as measured by para-aminohippurate.

From our data it is noted that the mean R.P.F. is decreased to 71.8 per cent of normal in patients with rheumatic valvular heart disease even before the classical signs of congestive failure develop. It has been clearly demonstrated previously[4,5] and confirmed by our investigations that there is a marked decrease in the effective renal plasma flow in patients with chronic congestive heart failure. During decompensation, as noted in Group C, the mean R.P.F. was reduced to 31.5 per cent of normal. With clinical compensation the mean R.P.F. was noted to increase approximately 67 per cent but still remained at a reduced rate of 53 per cent of normal. These findings are better exemplified in those patients who were studied both during congestive failure and again after clinical compensation was established (Table V). In six patients so studied the mean effective renal plasma flow increased 57 per cent with compensation.

Glomerular Filtration Rate (*G.F.*).—In the normal subjects (Table I) the mean glomerular filtration rate was 103 ± 7.4 ml. per minute. Although this is lower than the normal mean value established with inulin by Goldring and Chasis[6] and Merrill,[4] it is almost identical to the normal mean glomerular filtration rate established by Mokotoff and associates,[5] with the use of mannitol. In Group A the mean glomerular filtration rate of 101 ± 25.7 ml. per minute (Table II)

TABLE II. GROUP A. RENAL STUDIES IN PATIENTS WITH ORGANIC HEART DISEASE BUT NEVER CONGESTIVE FAILURE OR EDEMA

PATIENT	AGE	DIAGNOSIS OF HEART DISEASE	R. P. F.	G. F.	F. F.	Tm_{pah} MG. PER MIN. PER 1.73 SQ. M.	VITAL CAPACITY (LITERS)	VENOUS PRESSURE (CM.)	CIRCULATION TIME (SECONDS)
			ML. PER MIN. PER 1.73 SQ. M.		PER CENT				
E. L.	20	Rheumatic-M. S.-A. I.	377	90	23.8	91.0	3.2	7.3	20
K. F.	43	Rheumatic-M. S.-A. I.	338	86	25.4	57.3	3.2	6.0	—
M. W.	42	Rheumatic-A. I.	518	146	28.1	47.9	3.1	7.0	15
F. W.	26	Rheumatic-M. S.-A. I.	376	85	22.6	83.0	5.0	10.0	20
R. B.	22	Rheumatic-A. I.	556	96	17.2	86.4	4.6	—	12
Mean			433*	101*	23.4*	73.1			
Standard deviation			97.2	25.7	4.0	19.2			

R.P.F., G.F., F.F., and Tm_{pah} as in Table I; M.S. = mitral stenosis; A.I. = aortic insufficiency.
*Eight additional patients have now been added to this group without significantly altering the mean values for R.P.F., C.F. and F.F.

TABLE III. GROUP B. RENAL STUDIES IN PATIENTS WITH HEART DISEASE AND CONGESTIVE FAILURE. PATIENTS COMPENSATED AND WITHOUT EDEMA AT TIME OF STUDY

PATIENT	AGE	DIAGNOSIS OF HEART DISEASE	R. P. F.	G. F.	F. F.	$T_{M_{pah}}$	VITAL CAPACITY	VENOUS PRESSURE	CIRCULATION TIME
			ML. PER MIN. PER 1.73 SQ. M.		PER CENT	MG. PER MIN. PER 1.73 SQ. M.	(LITERS)	(CM.)	(SECONDS)
E. J.	29	Myocarditis (Influenzal)	444	97	21.8	97.1	4.8	6.0	19
P. R.	57	Arteriosclerotic	263	100	38.0	——	2.3	4.0	22
E. Da.	52	Arteriosclerotic	371	66	17.8	——	3.6	11.0	16
D. S.	24	Rheumatic	295	115	38.9	——	2.9	7.3	—
T. G.	32	Myocarditis (Fiedler's)	439	86	19.6	65.4	3.6	9.0	22
H. H.	25	Rheumatic-SBE.	300	93	31.0	78.4	2.7	12.6	19
L. F.	57	Rheumatic	264	65	24.6	68.2	3.2	7.5	18
C. H.	51	Atrial septal defect	250	78	31.2	44.5	2.8	7.0	18
C. V.	54	Arteriosclerotic	332	117	35.3	56.5	4.0	5.0	20
A. B.	56	Rheumatic	218	70	32.1	81.9	3.4	11.5	20
H. B.	52	Rheumatic	447	87	19.5	81.1	4.5	10.0	20
F. M.	36	Rheumatic	214	64	29.9	——	——	9.5	14
Mean			320	86	28.3	71.6		8.4	
Standard deviation			86.5	18.6	7.5	16.5		2.7	

SBE=subacute bacterial endocarditis.
For other abbreviations see Table I.

TABLE IV. GROUP C. RENAL STUDIES IN PATIENTS WITH HEART DISEASE AND CONGESTIVE FAILURE. PATIENTS DECOMPENSATED AT TIME OF STUDY

PATIENT	AGE	DIAGNOSIS OF HEART DISEASE	R. P. F.	G. F.	F. F.	$T_{M_{pah}}$	VITAL CAPACITY	VENOUS PRESSURE	CIRCULATION TIME	REMARKS
			ML. PER MIN. PER 1.73 SQ. M.		PER CENT	MG. PER MIN. PER 1.73 SQ. M.	(LITERS)	(CM.)	(SECONDS)	
P. R.	57	Arteriosclerotic	168	84	50.0	—	1.0	17.0	55	3+ edema
D. S.	24	Rheumatic	175	97	55.4	—	2.0	22.0	42	2+ edema
G. A.	56	Rheumatic	124	55	44.4	—	2.6	—	16	3+ edema
T. G.	32	Myocarditis	233	103	44.2	36.0	2.7	27.5	—	4+ edema
D. J.	58	Rheumatic	90	35	38.9	—	2.6	16.0	25	2+ edema
H. H.	25	Rheumatic	247	105	42.9	53.9*	2.4	12.0	30	1+ edema
H. G.	58	Rheumatic	232	64	28.0	79.7*	—	19.0	55	Râles
E. D.	56	Rheumatic	313	80	25.5	39.2	2.9	8.8	40	Chronic failure
R. Mc.	58	Arteriosclerotic	153	68	44.4	20.9	1.6	22.0	—	1+ edema
E. O.	56	Rheumatic	167	54	32.3	—	—	—	—	Trace edema
A. A.	48	Type undetermined	184	70	38.0	51.0*	3.0	14.4	47	2+ edema
M. O.	59	Rheumatic	162	67	41.4	42.2	—	19.3	—	Râles
M. K.	55	Rheumatic	220	92	41.8	31.0	2.8	24.0	35	Râles
Mean			190	75	40.5	44.2		18.4		
Standard deviation			58.2	20.9	8.3	17.8		5.5		

For abbreviations see Table I.

*In three cases the $\frac{\text{load}}{T_{pah}}$ ratio was less than 2.0 but greater than 1.5.

TABLE V. RENAL STUDIES IN PATIENTS WITH HEART DISEASE. COMPARISON OF FINDINGS ON SAME PATIENTS DURING CARDIAC FAILURE WITH PERIPHERAL EDEMA AND AFTER COMPENSATION AND DISAPPEARANCE OF EDEMA

PATIENT	AGE	DIAGNOSIS OF HEART DISEASE	R. P. F.		G. F.		F. F.		Tm_{PAH}		VENOUS PRESSURE CM.	
			ML. PER MIN. PER 1.73 SQ. M.				PER CENT		MG. PER MIN. PER 1.73 SQ. M.			
			CARDIAC FAILURE WITH EDEMA									
			PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT
E. E.	55	Rheumatic	211	388	—	—	—	—	—	—	25.0	8.0
E. J.	29	Myocarditis	318	444	—	—	—	—	—	—	17.5	6.0
P. R.	57	Arteriosclerotic	168	263	84	100	50.0	38.0	—	—	17.0	4.0
D. S.	24	Rheumatic	175	295	97	115	55.4	38.9	—	—	22.0	7.3
T. G.	32	Myocarditis	233	439	103	86	44.2	19.2	36.0	65.4	27.5	9.0
H. H.	25	Rheumatic	247	300	105	93	42.9	31.0	53.0	78.4	12.0	12.6
Mean			225	355	97	98	48.1	31.9	44.9	71.9	20.2	7.6

For abbreviations see Table I.

was not significantly different from the control value. The mean value for patients in Group B was 86 ± 18.6 ml. per minute (Table III). This represents a significant statistical difference as compared to the normal control group (P. less than 0.01). The mean rate of glomerular filtration for the Group C patients was 75 ± 20.9 ml. per minute (Table IV). As compared with Group B this does not represent a significant difference in the rate of glomerular filtration (P. less than 0.2 but greater than 0.1).

Early in the course of rheumatic heart disease the rate of glomerular filtration remains normal. In organic heart disease with chronic congestive failure the glomerular filtration rate was reduced to 72.8 per cent of normal. With clinical compensation there was no significant change in the rate of glomerular filtration. In four patients the mannitol clearance was determined during decompensation and again after clinical recovery and the mean rate of glomerular filtration remained unchanged (Table V).

Filtration Fraction (*G.F./R.P.F.*).—The mean filtration fraction for the control group was 17.4 ± 2.3 per cent (Table I). In all phases of heart disease there is a proportionately greater reduction of the renal plasma flow than of the glomerular filtration rate, manifesting itself by an increase in the filtration fraction. The mean value for Group A was 23.4 ± 4.0, which was significantly different from normal (P. less than 0.01). During congestive heart failure as noted in Group C the mean filtration fraction is greatly increased to 40.5 ± 8.3. With clinical compensation (Group B) the mean value was 28.3 ± 7.5 per cent, being significantly different from both Group C and normal (P. less than 0.01 for both comparisons).

Maximal Tubular Excretory Capacity (*Tm* $_{pah}$).—The Tm $_{pah}$ in seven normal male subjects was 80.3 ± 20.3 mg. per minute (Table I). This is comparable to the normal mean value of 77.5 ± 12.9 reported by Chasis and co-workers.[8] In the patients with rheumatic valvular heart disease who had never experienced congestive heart failure (Group A) the Tm $_{pah}$ was 73.1 ± 19.2 mg. per minute (Table II), which is not significantly different from normal. This was also found to be true for the patients who were admitted to the hospital in congestive failure but who were studied at a time when they were clinically compensated (Group B), the Tm $_{pah}$ for this group being 71.6 ± 16.5 mg. per minute (Table III). In sharp contrast, however, the Tm $_{pah}$ for patients studied during decompensation (Group C) was markedly reduced. The mean value for these patients was 44.2 ± 17.8 mg. per minute (Table IV). This decrement is highly significant when statistically compared with the normal control value for Tm $_{pah}$ (P. less than 0.01). In all cases in which Tm $_{pah}$ data is included the tubular load was determined as being adequate. Actually the $\frac{\text{load}}{T_{pah}}$ ratio was greater than 2.0 in all but three cases and in these three the ratio was greater than 1.5. From our data it is evident that the maximal tubular excretory capacity (Tm $_{pah}$) is reduced to 55 per cent of normal during chronic congestive failure but with clinical compensation there is a return to normal function. In only two patients was the Tm $_{pah}$ determined both during and after congestive heart failure. In these patients (T.G. and H.H.) the Tm $_{pah}$ returned to normal with compensation and further exemplified the changes noted in Groups B and C as a whole.

Venous Pressure.—In our series the mean venous pressure during congestive heart failure was 18.4 ± 5.5 cm. of saline (Table IV). With clinical recovery the mean venous pressure returned to a normal value of 8.4 ± 2.7 cm. saline (Table

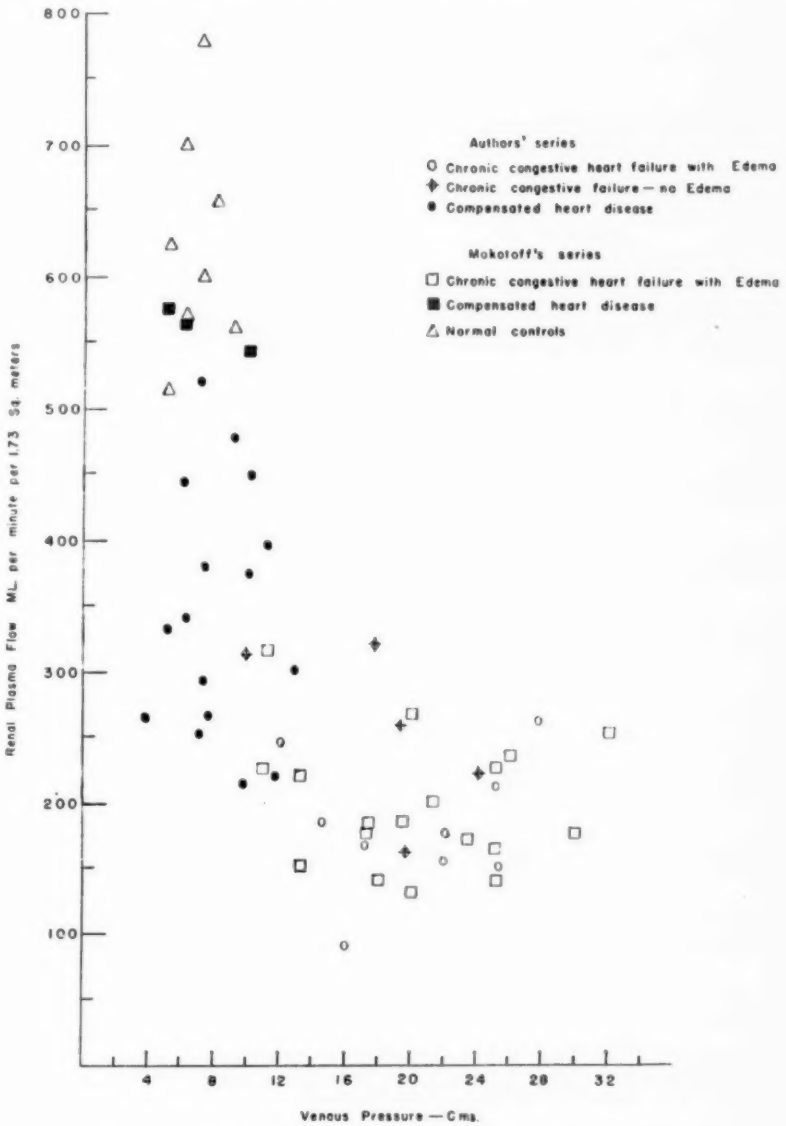

Fig. 1.—Correlation between renal plasma flow and venous pressure.

III) and as previously noted there was a 68.4 per cent increase in the mean effective renal plasma flow and a 62 per cent increase in the mean Tm_{pah}. These same changes are better demonstrated in those patients studied both during cardiac failure and again after clinical recovery (Table V). In these six patients

the mean venous pressure decreased from 20.2 to 7.6 cm. saline and the mean effective renal plasma flow increased 57.0 per cent. Merrill[4] has shown that among patients with chronic congestive heart failure there is an insignificant correlation between effective renal plasma flow and venous pressure. Similar analysis of our patients in Group C lends support to this conclusion. The correlation coefficient as determined only among the patients with congestive failure (Table IV) was −0.2169, which is not significantly different from zero. However,

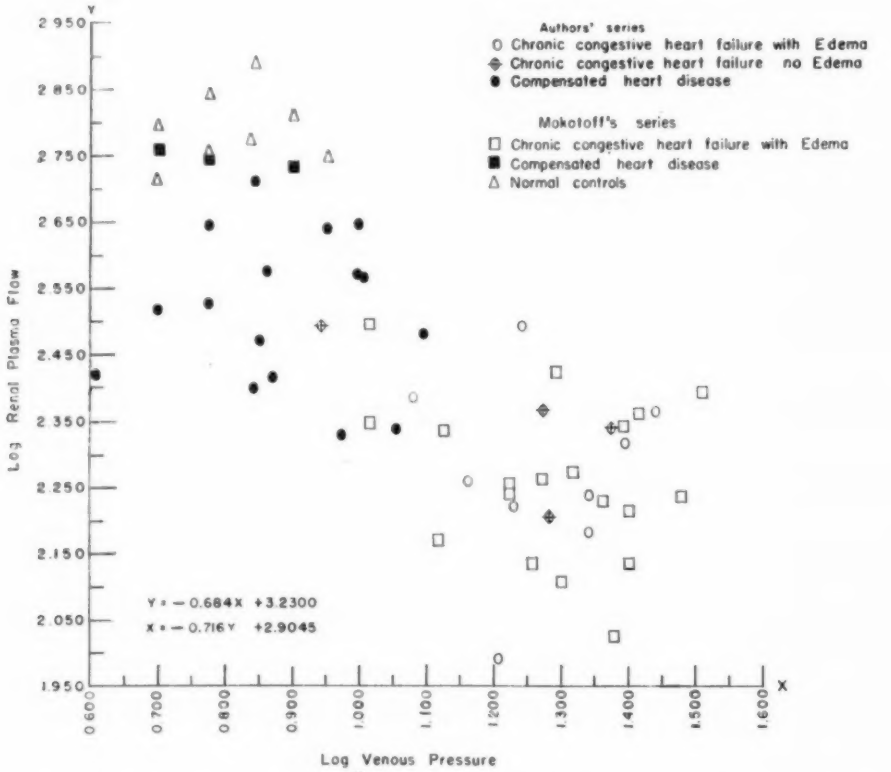

Fig. 2.—Correlation between log. renal plasma flow and log. venous pressure. Correlation coefficient r = −0.6969, P. less than 0.01 indicating a significant degree of correlation.

if one correlates the effective renal plasma flow and venous pressure among all groups combined, then a significant inverse relationship is found to exist. In order to make the results more significant we have included the data given by Mokotoff and associates[5] and have plotted the combined data graphically as shown in Fig. 1. When the logarithms of these values are plotted graphically (Fig. 2), the relationship is approximately linear with a correlation coefficient of −0.6969. The probability that this is a chance difference from zero is less than 0.01.

The changes in the renal hemodynamics before heart failure, during congestive failure, and after clinical compensation are shown graphically in Fig. 3.

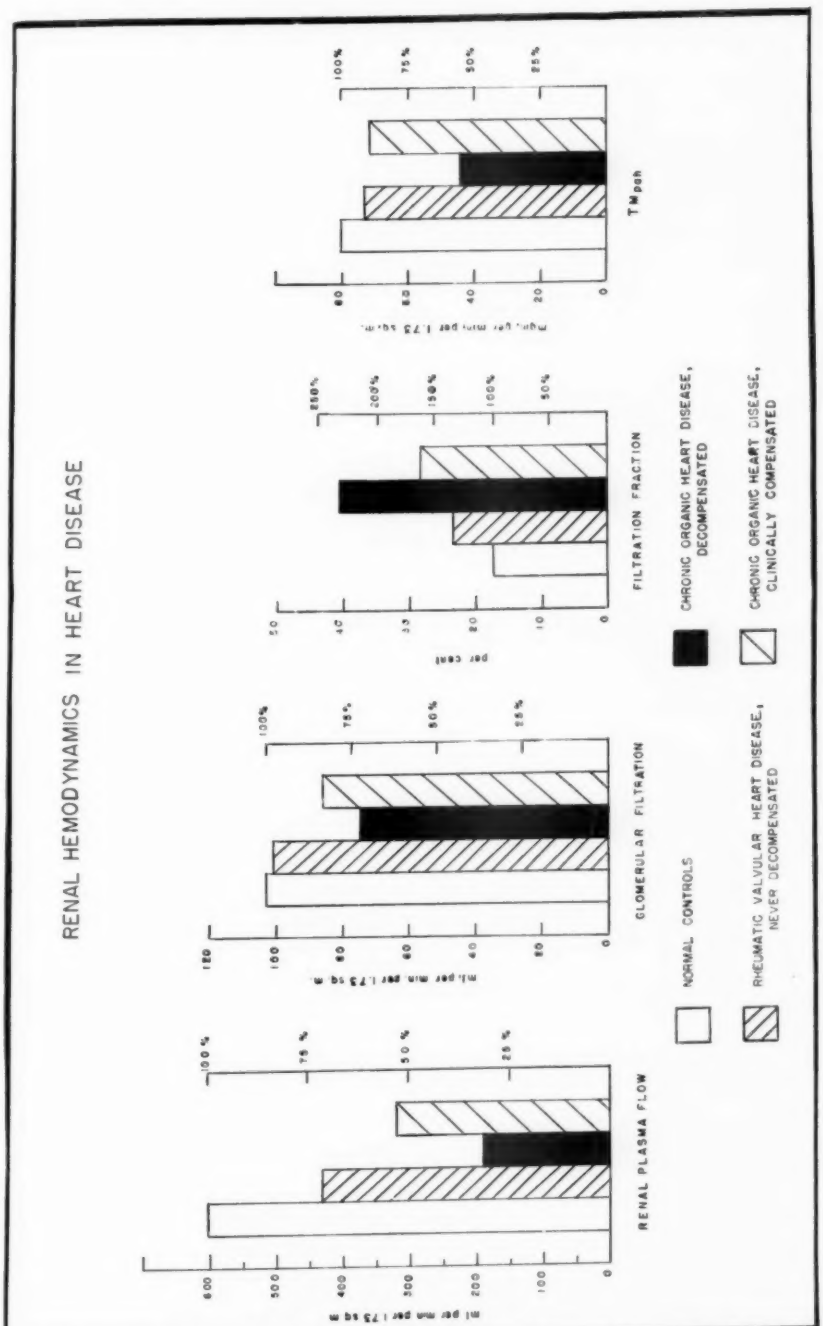

Fig. 3.—The effective renal plasma flow, rate of glomerular filtration, filtration fraction, and maximal tubular excretory capacity in normal control subjects and patients with organic heart disease.

DISCUSSION

The changes in the effective renal plasma flow constitute the most striking disturbance of the renal hemodynamics in patients with organic heart disease. Of considerable interest was the finding of a diminished renal plasma flow in patients with rheumatic valvular heart disease who had never experienced heart failure. This finding was associated with a normal rate of glomerular filtration and a normal value for the maximal tubular excretory capacity for para-aminohippurate. The decrease in the effective renal plasma flow may represent one of the earliest hemodynamic changes in compensated valvular heart disease and indicates a shunt of blood from the kidneys even before the classical symptoms of congestive failure occur. The marked reduction of the effective renal plasma flow in congestive heart failure has been demonstrated previously[4,5] and has been confirmed by our investigations. With clinical compensation the renal plasma flow increases from that noted during decompensation but remains markedly reduced from normal and significantly less than that noted before the onset of congestive failure.

A reduction of the effective renal plasma flow might conceivably be due to: (1) decreased arterial pressure, (2) increased venous pressure, or (3) renal arteriolar vasoconstriction. The arterial pressure is probably of little importance in this regard and was not found to differ significantly among the groups of patients studied. The role of increased venous pressure in the pathogenesis of decreased effective renal plasma flow has been a matter of dispute in the recent literature.[4,5,13] Merrill[4] has stated that a reduction of venous pressure to normal with mercurial diuretics has no effect on the renal blood flow and has thus concluded that increased venous pressure is not a factor responsible for the decreased renal blood flow in congestive failure. On the other hand, Bradley and Bradley[13] have shown that by increasing the intra-abdominal pressure in normal subjects they were able to increase the mean renal venous pressure to 18.3 mm. Hg (24.9 cm. water), and concomitantly noted a decrease in the effective renal plasma flow, rate of glomerular filtration, and maximal tubular excretory capacity. It was concluded, therefore, that on the basis of their average data, the increase of renal venous pressure was usually sufficient to account for the reduction of effective renal plasma flow. Although there exists a relationship between venous pressure and renal plasma flow in patients with organic heart disease, it is obvious that the reduction in renal plasma flow is not caused primarily by changes in the venous pressure. It is conceivable that in patients with congestive heart failure an increased pressure in the venular end of the capillary bed might be a minor factor responsible for the reduction in the effective renal plasma flow.

In all phases of heart disease studied there was a disproportionate reduction in the effective renal plasma flow and rate of glomerular filtration. Thus it has been shown that in patients with congestive heart failure the renal plasma flow may be 20 to 30 per cent of normal and the rate of glomerular filtration reduced to only 66 to 75 per cent of normal. The maintenance of the glomerular filtration rate at a relatively high level in the presence of the great reduction of the renal plasma flow suggests a high degree of efferent arteriolar spasm which increases the effective intraglomerular pressure. This is reflected in the markedly

elevated filtration fraction, and thus in congestive heart failure there is a considerably greater percentage of the plasma filtered per minute than occurs in normal subjects. The increased filtration fraction suggests that renal efferent arteriolar vasoconstriction is a prominent feature of all phases of organic heart disease. The mechanism of this vasospasm is unknown.

The relationship of effective renal plasma flow to cardiac output in all of the phases of heart disease cannot be completely evaluated at this time; however, it is of importance to note that Stewart and colleagues[10] have previously demonstrated a reduction in the cardiac index in patients with compensated rheumatic valvular heart disease without previous evidence of heart failure. Furthermore Merrill[4] has shown that there is a significant correlation between cardiac output and renal plasma flow during congestive heart failure. However, the reduction in the renal plasma flow is proportionately greater than the reduction in the cardiac output and suggests that a renal regulatory mechanism produces a significant shunt of blood from the kidneys. The pathways by which this mechanism is mediated are unknown.

It seems to have been generally conceded that tubular function is normal in congestive heart failure.[12,14] This assumption has been based primarily on the observation that the kidneys are able to concentrate the urine in heart failure. It is, therefore, of extreme interest to note that there is a marked reduction in the maximal tubular excretory capacity for para-aminohippurate in decompensated patients, whereas it is normal in patients who are clinically compensated. Although it has been considered that the Tm_{pah} is a measure of the quantity of tubular mass,[6,7] it is obvious that this relationship does not apply in congestive heart failure. The Tm_{pah} is actually a measure of the excretory capacity of the tubules and in no way can it be construed to indicate an anatomic number of nephrons. The fact that the Tm_{pah} reverts to normal with clinical compensation further emphasizes the functional aspects of this phenomenon. The specific mechanism involved in the decrement of the maximal tubular excretory capacity during congestive heart failure is unknown. The mechanisms which might conceivably be invoked are as follows: (1) an anatomic reduction of the number of nephrons, (2) intermittent glomerular occlusion, (3) blockage of "low pressure" nephrons by elevated venous pressure, (4) a specific loss of the tubular capacity to excrete para-aminohippurate, and (5) efferent arteriolar spasm of a severe degree resulting in tubular ischemia.

The first hypothesis is untenable as it has been demonstrated that the maximal tubular excretory capacity returns to normal with the restoration of clinical compensation.

Intermittent glomerular activity has been shown to be an unlikely occurrence in the normal human kidney[7] and it is improbable that this mechanism occurs in congestive heart failure. Furthermore, there is no evidence to suggest that afferent arteriolar spasm is a prominent feature during heart failure.

Bradley and Bradley[13] have stated that the reduction of maximal tubular excretory capacity noted during increased intra-abdominal pressure is due to the increased renal venous pressure and related increased intrapelvic pressure. These factors would result in blockage of urine flow from "low pressure" nephrons.

These authors state that the inactive nephrons would not contribute to the clearance of mannitol but the blood could be cleared of para-aminohippurate by neighboring operative tubules. If the reduction of the Tm_{pah} to 55 per cent of normal were due to blockage of urine from "low pressure" nephrons, then one must assume that 45 per cent of the glomeruli are inactive. Since the mean filtration fraction in this group of patients was 40.5 per cent, it is apparent that the filtration fraction in the active glomeruli would have to attain exceedingly high values, probably in the range of 70 to 80 per cent. As noted by Smith and his associates[15] it is unlikely that such high values could be attained.

The hypothesis that the decrement in the maximal tubular excretory capacity in congestive heart failure is due to a specific inability of the tubules to excrete para-aminohippurate cannot be evaluated at this time. It is known that this function may be reduced early in essential hypertension even though the renal plasma flow and rate of glomerular filtration are normal.[6] It is also known that other factors can influence the excretory function of the tubules. Hypophysectomy has been shown to decrease the maximal tubular excretory capacity and vitamin A and testosterone to increase this function.[6]

The reduction in the maximal tubular excretory capacity in heart disease occurs in the patients with the highest filtration fraction, that is, in those patients with the most marked degree of efferent arteriolar spasm. The assumption that this vasoconstriction might be so intense in localized areas of the kidneys as to result in renal ischemia and an actual decrease in the functional capacity of the tubules seems to be logical. If this mechanism is assumed to occur, one would expect to show that true renal ischemia occurs in congestive heart failure. That this actually does occur has been shown by Merrill[4] who reported an increase in the arteriovenous oxygen differences in patients with congestive heart failure. Therefore, it seems likely that this single mechanism, which correlates well with the other observed changes in renal hemodynamics in congestive heart failure, might also be primarily responsible for the reduction in maximal tubular excretory capacity.

Though this study touches only indirectly upon the problem of the pathogenesis of cardiac edema, some interesting deductions can be formulated relative to this problem. There are obviously only two fundamental mechanisms by which the urinary excretion of sodium is controlled: namely, the rate of glomerular filtration and the amount of tubular reabsorption of sodium. Merrill[4,11] and Mokotoff and his associates[5] postulate that sodium retention is due primarily to a reduced rate of glomerular filtration. If this were true, one would expect to find a significant difference in the glomerular filtration rates of the edematous and nonedematous patients with chronic heart failure. Since the volume of the glomerular filtrate is significantly reduced in chronic congestive heart failure, it is apparent that the amount of sodium presented to the tubules is also reduced. Thus this mechanism is certainly involved in the retention of salt and water. However, since the disappearance of edema associated with clinical compensation is not correlated with a significant increase in the rate of glomerular filtration in our patients, the operation of another mechanism for salt and water retention is suggested. In our patients the rate of glomerular filtration is not significantly

changed as edema disappears, but there is a very significant increase in the renal plasma flow and a fall in the filtration fraction. In 1942 Seymour and his coworkers[12] noted similar changes in the renal function of six patients recovering from congestive heart failure: namely, the rate of glomerular filtration (inulin clearance) showed no significant change, but the renal blood flow (phenol red clearance) increased to a degree approximating the increase in cardiac output. This suggests that in addition to decreased sodium filtration in heart failure there must also be an increase in the percentage of sodium reabsorption by the tubules. That tubular dysfunction exists in congestive heart failure is shown by the reduction of Tm_{pah}. However, owing to the well-known dissociation of tubular reabsorption and excretion,[6,7] the Tm_{pah} cannot be used as a criterion of the tubular reabsorption of sodium. It is conceivable that the markedly elevated filtration fraction noted in congestive heart failure might so disturb osmotic relationships in the kidney that the tubular reabsorption of sodium is enhanced. This hypothesis cannot be evaluated without further investigation of the mechanisms by which sodium excretion and retention occur in both normal persons and patients with heart disease.

SUMMARY AND CONCLUSIONS

1. The renal hemodynamics have been studied in twenty-six patients with organic heart disease by the utilization of the mannitol and para-aminohippurate clearance techniques for the determination of the effective renal plasma flow, rate of glomerular filtration, and maximal tubular excretory capacity.

2. The effective renal plasma flow is significantly decreased in patients with rheumatic valvular heart disease even before the classical signs of congestive heart failure occur. During congestive heart failure there is a marked reduction of the renal plasma flow. With clinical compensation there is a significant increase, but the mean value still remains considerably below normal. The mechanisms which might be operative in producing changes in renal plasma flow in heart disease are discussed.

3. In patients with rheumatic valvular heart disease who have never experienced congestive failure the rate of glomerular filtration remains normal. In patients studied during congestive heart failure there is a significant reduction in the glomerular filtration rate, and this does not change significantly with clinical compensation. The changes in the effective renal plasma flow are disproportionately greater than those noted in the glomerular filtration rate, thus resulting in an increased filtration fraction in all phases of heart disease. The increase in filtration fraction is greatest in patients with congestive heart failure. This is indicative of a marked degree of efferent arteriolar spasm.

4. The tubular excretory capacity for para-aminohippurate is markedly reduced in patients with clinical decompensation but is normal in other phases of heart disease. The factors which might conceivably be involved are discussed, and it seems that intense renal ischemia is the most likely cause.

We are indebted to Dr. R. V. Ebert, Chief of the Medical Service, and Dr. H. S. Wells, Director of Research, for their advice and help in making this work possible. We also thank Dr. L. Zieve for aid in the statistical treatment of the data and Mrs. Barbara Jarl for her technical assistance.

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A CRITICAL EVALUATION OF EXTREMITY AND PRECORDIAL ELECTROCARDIOGRAPHY IN ACUTE COR PULMONALE

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AN electrocardiographic-pathologic correlation was recently made of 150 consecutive patients who had at least one complete set of unipolar limb and chest leads during their final hospitalization.[1] The electrocardiographic diagnosis of acute cor pulmonale was made in eight of these individuals. A critical analysis of these observations is presented in this report.

The criteria for the diagnosis of acute cor pulmonale in the standard electrocardiographic leads have been established by McGinn and White[2] and Murnaghan, McGinn and White.[3] These consist of the development of S_1, depression of RS-T_1 and RS-T_2 with staircase effect, lowering of T_2, development or deepening of Q_3, inversion of T_3 with elevation of RS-T_3 and inversion of T waves in certain precordial leads. More recently others have emphasized the inversion of the T waves over the right ventricle,[4-6] shift of the transitional zone to the left,[7] the development of an R or R′ wave in the unipolar right-arm lead, and transient incomplete right bundle branch block.[6,8]

In the present group characteristic or suggestive changes developed in the conventional leads in four instances, were limited to the unipolar chest leads in one instance, and in two others equivocal changes in the standard leads were supported by characteristic changes in the precordial leads. Four of these patients showed incomplete right bundle branch block, a diagnosis which can only be made with certainty if late activation of the right ventricle is established by the precordial leads.[7,9] Two patients showed a shift of the transitional zone to the left. An R wave developed in aV_R in two. Necropsy confirmed the diagnosis in these seven subjects.

The diagnosis of acute cor pulmonale was favored over that of posterior myocardial infarction in the eighth patient because the Q wave in Lead aV_F was small.[10] The unipolar chest leads were normal. Autopsy showed posterior myocardial infarction but no pulmonary infarct or embolus. In a ninth patient, acute cor pulmonale was favored over subendocardial myocardial infarction, but the latter was found at autopsy. This example is more fully described in a separate communication.[11]

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Post-mortem examination showed pulmonary infarcts or embolism in seven additional patients, but electrocardiograms were taken in only one of these patients during the acute terminal episode. In this subject the electrocardiogram was characteristic of left ventricular hypertrophy and showed no suggestive or diagnostic evidence of acute cor pulmonale. An embolus was found in the right pulmonary artery one day after the tracing was made. Since electrocardiograms were not taken at the presumed time of embolization in the other six patients they could not be expected to show diagnostic changes and are therefore not considered further.

We were impressed in this study with the value of the electrocardiogram in establishing or suggesting the diagnosis of pulmonary embolism for the first time. The following protocols illustrate the clinical and electrocardiographic variations of acute cor pulmonale, emphasize the important place of the electrocardiograms in this diagnosis, and demonstrate the invaluable role of precordial electrocardiography in confirming or establishing the diagnosis.

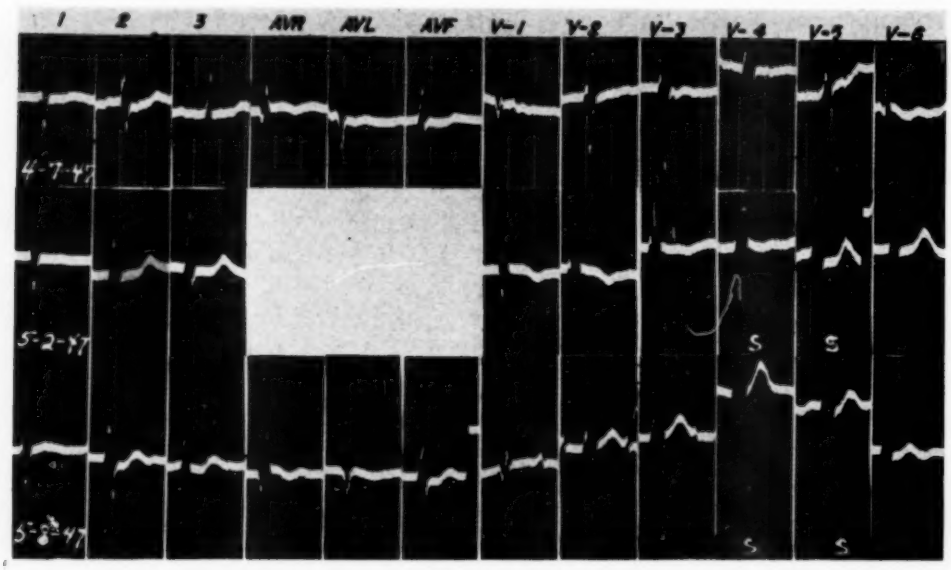

Fig. 1.—Case 1. Acute cor pulmonale in a 58-year-old man with rheumatic mitral and aortic stenosis and insufficiency in acute congestive failure.

Upper tracing: Right axis deviation, late intrinsicoid deflection of ventricular complex in V_1. *Middle tracing:* This was taken during an attack of acute dyspnea. Chest leads show incomplete right bundle branch block with inverted T waves in V_1 through V_3. Note lack of significant change in standard leads. *Lower tracing:* This was taken six days later. It shows return toward original form. Transitional zone remains at V_6. Autopsy showed multiple recent and old pulmonary infarcts.

CASE REPORTS

Case 1 (P.B.B.H., H1185).—A.P., a 58-year-old man with rheumatic mitral and aortic stenosis and insufficiency was admitted to the Peter Bent Brigham Hospital on April 7, 1947, for an acute exacerbation of chronic congestive failure. An electrocardiogram on admission (Fig. 1) showed paroxysmal auricular tachycardia with block, ventricular premature beats, and right axis deviation with the heart in the vertical position. Lead aV_R showed a Q wave followed

by a large R wave. Unipolar chest leads showed a late ventricular intrinsic deflection in V_1. The auricular deflections showing paroxysmal auricular tachycardia were apparent only in V_1 and V_2. The patient became worse during his hospital admission and had frequent episodes of acute dyspnea. A tracing taken at the height of one of these episodes showed typical incomplete right bundle branch block, the QRS complex measuring 0.11 second. The transitional zone (the point on the precordium where the QRS complexes change from predominantly downward to predominantly upward) was between V_3 and V_4 (Fig. 1). Unipolar limb leads were not taken. The patient continued to do badly in spite of appropriate therapy. A tracing six days later showed a sinus tachycardia (rate 120), depressed RS-T_2 and RS-T_3 and a biphasic T_3. Unipolar limb leads continued to show a prominent R wave in aV_R, and a depressed RS-T segment in aV_F. Unipolar chest leads showed incomplete right bundle branch block. The transitional zone was at V_6 (Fig. 1). Subsequent electrocardiograms were similar. The patient died on May 20, 1947, in acute respiratory distress. Autopsy showed rheumatic heart disease and multiple recent and old pulmonary infarcts. The left femoral vein and the periprostatic plexus were the source of the emboli.

CASE 2 (P.B.B.H., 1A149).—M.H., an 81-year-old woman, sustained multiple fractures of the left hip and humerus on April 6, 1947, for which she was admitted to the hospital. She was treated with traction. Roentgen-ray examination of the chest showed slight cardiac enlargement. An electrocardiogram on April 8, 1947, showed incomplete right bundle branch block,

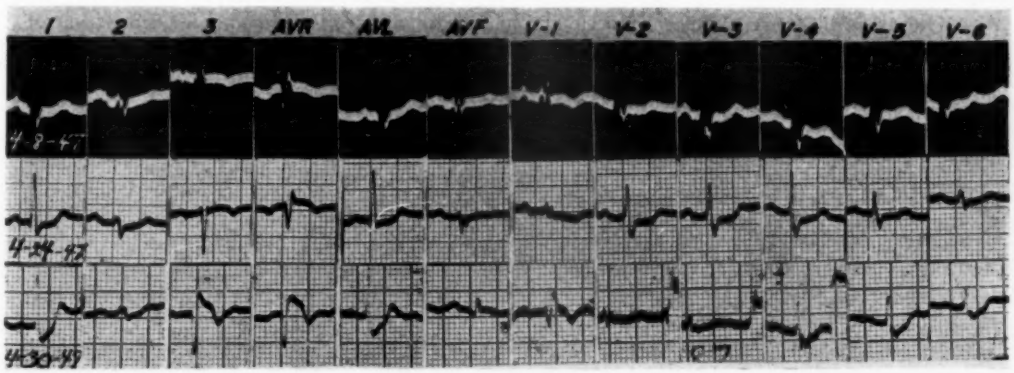

Fig. 2.—Case 2. Acute cor pulmonale in an 81-year-old woman with fractured hip.
Upper tracing: Taken because of cardiac enlargement. This shows incomplete right bundle branch block. *Middle tracing:* Taken one hour after onset of acute dyspnea. The RS-T segments in Leads I, II, and aV_L, are slightly depressed. *Lower tracing:* Taken six days later during recurrent dyspnea and chest pain. This shows marked depression of the RS-T segments in Leads I, aV_L, and V_4 through V_6; elevated RS-T in Leads III and aV_R; deep Q_3 and a broad, relatively prominent Q wave in aV_F; V_2 through V_4 understandardized. Diagnosis of acute cor pulmonale made in face of relatively prominent Q wave in Lead aV_F. Autopsy showed pulmonary embolus and old infarcts of both lungs. No myocardial infarct.

the QRS complex measuring 0.11 second. The R wave in aV_R was almost as prominent as the Q wave. There was an M-shaped QRS with a late intrinsicoid deflection in V_1 (Fig. 2). On April 24, eighteen days after admission, the patient suddenly complained of chest pain and dyspnea. An electrocardiogram at this time showed a prominent S_1 and S_2 with depression of the RS-T segment in Leads I, II, and aV_L. The RS-T segments were somewhat more depressed in V_2 through V_6, but there was no change in T waves or transitional zone (Fig. 2). These changes were noted but a definite electrocardiographic diagnosis of acute cor pulmonale was not made at that time.

The patient improved but six days later complained again of chest pain and dyspnea. At this time there was prominence of S_1 and S_2, elevation of RS-T_3 with late inversion of T_3. Unipolar limb leads showed elevation of the RS-T segment with late inversion of the T wave in aV_R, a prominent Q wave in aV_F measuring 0.03 second in duration and exceeding the following R wave

in amplitude. The T wave in aV_F was inverted. The unipolar chest leads were unsatisfactory due to understandardization and alternating current interference but showed late intrinsicoid deflection of the ventricular complex in V_1, no displacement of the transitional zone, and a prominent S wave and depression of the RS-T segment in V_4 through V_6 similar to that seen in Leads I and aV_L (Fig. 2).

The patient died six days later of respiratory failure. Autopsy showed a massive pulmonary embolus and old infarcts in the lower lobes of both lungs. Thrombi were found in the left femoral and iliac veins. The heart showed marked coronary sclerosis with diffuse left ventricular and septal scarring but no acute infarction.

Here was an instance of repeated pulmonary infarctions following fracture of the hip in an elderly woman with coronary arteriosclerotic heart disease. The incomplete right bundle branch block noted initially was probably due to myocardial scarring. Later the RS-T segment depressions in Leads I, aV_L, and V_4 through V_6 and the inversion of T_3 constituted the decisive electrocardiographic evidence of acute cor pulmonale. It is of considerable interest that this patient developed a prominent Q wave in aV_F.[12,13]

CASE 3 (P.B.B.H., G6983).—E.M., a 46-year-old housewife, was admitted to the hospital on July 7, 1947, for repair of a cystocele and umbilical hernia. There was no evidence of heart disease. Surgery was performed on July 8 and July 14. Five days after the second operation, while returning from the bathroom, the patient fell to the floor but could not explain why this occurred. An electrocardiogram on that day was not remarkable (Fig. 3). The T waves were

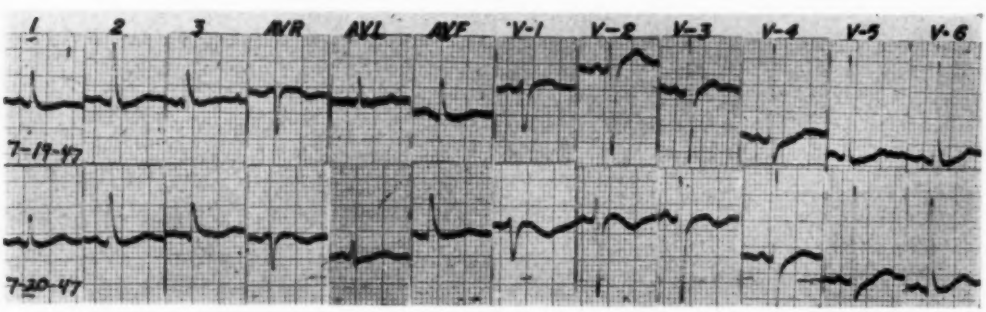

Fig. 3.—Case 3. Acute cor pulmonale in a 46-year-old woman with umbilical hernia.

Upper tracing: Taken five days postoperatively when patient collapsed. There were no changes typical of acute cor pulmonale. *Lower tracing:* Taken the following day. Conventional leads show no significant changes. Lead aV_L shows development of an S wave and minimal depression of the RS-T segment. Decisive changes present in precordial leads which show marked inversion of T wave in V_1 through V_3. The patient died the following day. Autopsy showed a recent infarct in the left lower lobe and massive pulmonary embolus.

slightly biphasic in all conventional leads and in aV_F, they were low in V_5 and V_6, and the RS-T segments were minimally depressed in V_4 through V_6. On the following day the patient complained of pain in the left side of the chest. This was ascribed to trauma incident to the fall. Nevertheless an electrocardiogram was taken later that day. There was no change in the conventional and unipolar limb leads, but the T wave was distinctly inverted in V_1 through V_3. The transitional zone remained between V_3 and V_4 (Fig. 3).

The next morning while getting out of bed the patient collapsed, became cyanotic, and died within twenty minutes. Post-mortem examination showed a massive embolus occluding the trunk of the pulmonary artery and a recent infarct in the lower lobe of the left lung. A thrombus was found in the left popliteal vein. The heart was normal.

In this patient the electrocardiographic evidence of acute cor pulmonale was the inversion of the T waves in V_1 through V_3. There was no apparent change in the position of the interventricular septum or change consistent with backward displacement of the apex of the left ventricle. The small Q_3 present in the first tracing showed no change.

CASE 4 (P.B.B.H., 6A730).—F.M., a 65-year-old woman, was admitted to the hospital in an acute exacerbation of long-standing congestive heart failure due to hypertensive heart disease. An electrocardiogram on admission (Fig. 4) showed auricular fibrillation with a ventricular rate of 112, left axis deviation, and depressed RS-T segments and low, biphasic T waves in Leads I, aV_L, V_4, and V_5. The QRS complex measured 0.08 second. The patient did well on usual therapy and was discharged improved. Two months later (Nov. 9, 1947) she was readmitted because of the abrupt development of severe dyspnea, orthopnea, and cyanosis. There was no chest pain. The cervical veins were engorged. The respiratory rate was 32. There was bilateral pulmonary edema. It appeared that the patient had suffered an acute break in compensation. An electrocardiogram on the following morning (Fig. 4) showed incomplete right bundle branch block (QRS duration was 0.11 second). S_1 was prominent. In Lead aV_R the Q wave had become smaller and the R wave was very prominent. In aV_L the RS-T segment had become depressed and the T wave low. Some of the complexes showed a Q wave in V_1 and V_2. V_4 showed a small Q wave. The R wave was smaller in V_3 than in V_2. The transitional zone was displaced beyond V_6. The T wave was low and notched in V_4 through V_6.

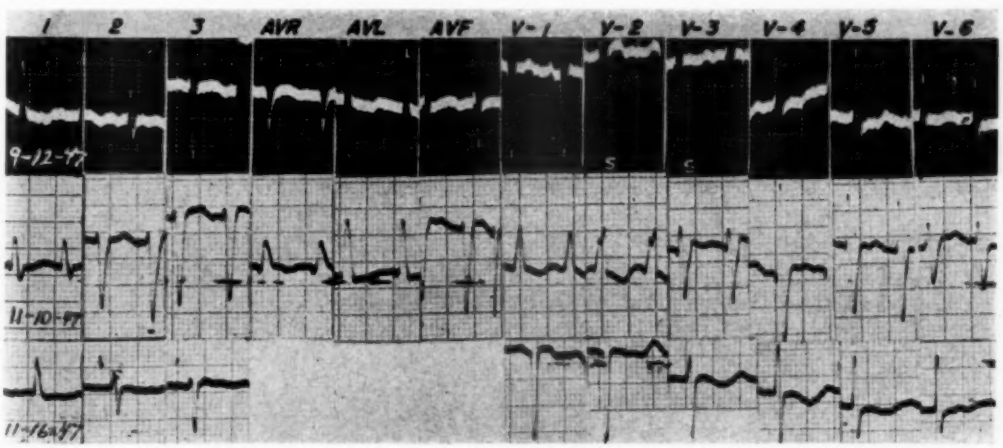

Fig. 4.—Case 4. Acute cor pulmonale in a 65-year-old woman with hypertensive heart disease and congestive failure.

Upper tracing: This was made on the first admission. It shows auricular fibrillation, depressed RS-T segments and biphasic T waves in Leads I, aV_L, and V_4 and V_5. *Middle tracing:* This was made on the second admission, one day after onset of acute dyspnea and cyanosis. It shows incomplete right bundle branch block. *Lower tracing:* Taken six days after the middle tracing. It shows return toward original form. The patient died six days later. Autopsy showed multiple pulmonary infarcts and cardiomegaly.

The patient continued to do poorly and was obviously jaundiced one week later. At this time an electrocardiogram showed a return to the original form in the standard leads, and the return of the transitional zone to between V_3 and V_4. The T wave became prolonged and biphasic in V_2 through V_5. The heart rate had slowed to 86. Unipolar limb leads were not taken (Fig. 4).

In spite of the fact that the patient had apparently recovered from this episode, she went progressively downhill and died on Nov. 22, 1947.

Post-mortem examination showed old and recent infarcts of all lobes of the right lung and of the lower lobe of the left lung. There was a fresh embolus in the artery to the lower lobe of the left lung. The heart weighed 440 grams and showed calcific aortic stenosis and hypertrophy of the left ventricle. There were thrombi in the right auricle and in both superficial femoral veins.

Here was a patient in whom the abrupt break in compensation was due to acute cor pulmonale and in whom the electrocardiographic finding of incomplete right bundle branch block was the first clear evidence of pulmonary infarction. This patient also demonstrated transient changes in the electrical position of the heart with displacement of the transitional zone to the left and changes which have been interpreted as due to posterior displacement of the cardiac apex.[10]

CASE 5 (P.B.B.H., 3A800).—M.L., a 52-year-old housewife, was admitted to the hospital on Nov. 26, 1947, because of acute intestinal obstruction. Physical examination showed no evidence of heart disease. Laporatomy was performed and carcinoma of the ovary with widespread metastases were found. A palliative procedure was carried out. Eight days postoperatively the patient developed the signs and symptoms of thrombophlebitis but had no respiratory symptoms. An electrocardiogram on that day revealed no abnormality (Fig. 5). There was a prom-

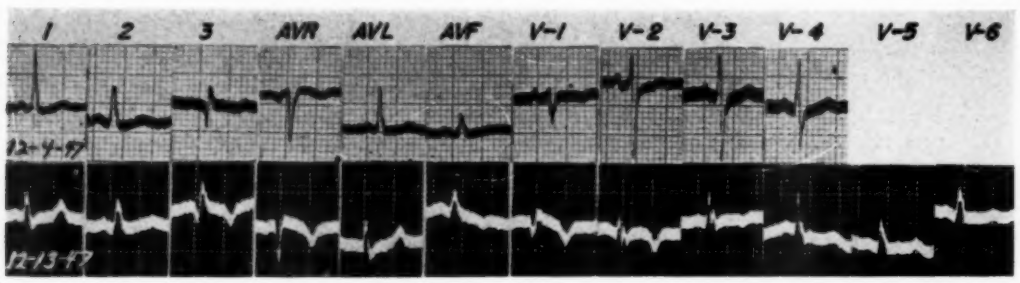

Fig. 5.—Case 5. Acute cor pulmonale in a 52-year-old woman with carcinoma of the ovary.

Upper tracing: Taken because of postoperative thrombophlebitis without respiratory symptoms. This shows a prominent Q wave in Lead III interpreted as normal in view of an absent Q wave in aV_F. *Lower tracing:* Taken seventeen days following surgery, immediately after onset of chest pain and dyspnea. This shows incomplete right bundle branch block. The patient died three hours later. Autopsy showed massive pulmonary embolus, normal heart.

inent Q_3 but no significant Q wave in aV_F. Both common femoral veins were ligated; clots were found on both sides. Nine days later the patient suddenly developed dyspnea and pain in the left side of the chest. An electrocardiogram taken immediately showed the development of an S wave and slight depression of the RS-T segments in Leads I and aV_L. Q_3 became broader (0.04 compared to 0.03 second) but less prominent relative to R_3. The T wave in Leads III and aV_F were now distinctly inverted and a small Q wave developed in aV_F. Unipolar chest leads showed late intrinsicoid deflection of the ventricular complexes in V_1 through V_3, suggesting incomplete right bundle branch block, and the T waves were inverted in these leads (Fig.5).

The patient died three hours later in acute pulmonary edema. Autopsy showed a massive embolus in the main pulmonary artery. The lungs showed only pulmonary edema. The heart was normal.

In this instance a control electrocardiogram was taken because of postoperative thrombophlebitis and was repeated following a single, eventually fatal, pulmonary embolization. The tracings showed characteristic changes in the standard leads and incomplete right bundle branch block with T wave inversion in Leads V_1 through V_3.

CASE 6 (P.B.B.H., L1785).—A.C., a 67-year-old spinster, was admitted to the hospital on Feb. 18, 1948, because of a fractured wrist. Examination disclosed a carcinoma of the breast. She gave no history suggestive of angina pectoris or myocardial infarction. An electrocardiogram, taken because of the presence of hypertension, showed a deep QS wave in Leads III, aV_F, and aV_R. T_3 was low but upright. The transitional zone lay between V_2 and V_3 (Fig. 6). A radical mastectomy was performed on Feb. 25, 1948. Two weeks postoperatively the patient suddenly went into shock and developed cyanosis, tachypnea, and râles in the lower lobe of the left lung. An electrocardiogram at this time showed low voltage with prominent S_1, QS_2, and QS_3, slight depression of RS-T_1, elevation of RS-T_2 and RS-T_3, and inversion of T_3. Unipolar limb leads showed an R wave of about the same magnitude as the Q wave in aV_R. Lead aV_L showed an S wave and depression of the RS-T segment. A small W-shaped QS complex in Lead aV_F was present. The only unipolar chest lead taken, V_4, was remarkable in that it showed an R wave which was much smaller than the S wave, indicating a shift of the transitional zone to the left of V_4 (Fig. 6).

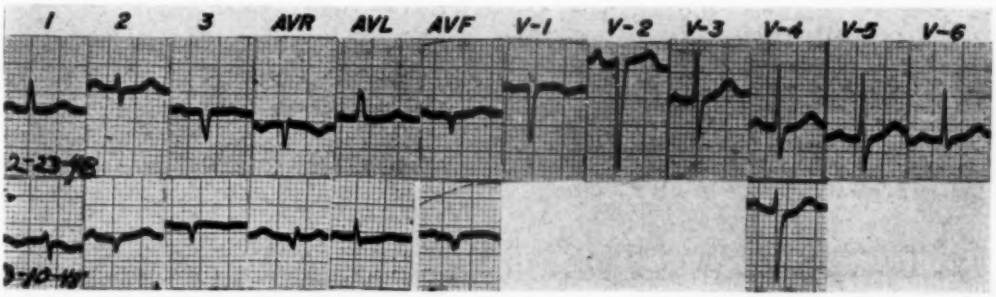

Fig. 6.—Case 6. Acute cor pulmonale in a 67-year-old woman with carcinoma of the breast.

Upper tracing: Preoperative electrocardiogram shows a QS complex in leads III and aV_F, interpreted as suggestive evidence of old posterior myocardial infarction. *Lower tracing:* Taken two weeks postoperatively because of shock and tachypnea. This shows development of an S_1, QS_2 and QS_3, slight depression of the RS-T segment in Lead I, and very slight elevation of the RS-T segment in Leads II and III; a large R wave in aV_R, depressed RS-T and persistent QS complex in Lead aV_L; shift of transitional zone to left of V_4. The patient died eight hours later. Autopsy showed pulmonary emboli and old posterior myocardial scar.

The patient died eight hours later without rallying. Autopsy showed emboli in both pulmonary arteries and a fresh infarct in the lower lobe of the left lung. There was an old scar, 1.5 cm. in diameter, in the posterior wall of the left ventricle of the heart. The leg veins were not examined.

This report illustrates that stigmata of acute cor pulmonale can manifest themselves when tracings have already shown evidence of posterior myocardial infarction. The depression of the RS-T segment in Leads I and aV_L, the development of an S wave in Leads I and aV_L and of an R wave in Lead aV_R, and the shift of the transitional zone to the left, constituted convincing evidence of acute cor pulmonale. The development of acute cor pulmonale did not mask the changes due to the old posterior myocardial infarct.

CASE 7 (P.B.B.H., 5A490).—N.S., a 56-year-old South African business man, was admitted to the hospital on March 10, 1947, because of chest pain of years' duration and renal colic. Physical examination revealed no abnormality except for the presence of râles and wheezes in both lungs. Pyelography showed bilateral renal calculi. An electrocardiogram on the day following admission showed no abnormality (Fig. 7).

Two days following a right nephrectomy the patient became intensely dyspneic after vomiting and went into shock. An electrocardiogram at this time showed that S_1 had become more prom-

inent, T_2 lower, and T_3 inverted. Unipolar limb leads now showed a prominent Q wave in aV_F measuring 0.03 second in duration and equaling the following R wave in magnitude, while the T wave became inverted. The unipolar chest leads showed that the transitional zone had shifted to V_6. The T wave became inverted in V_1 (Fig. 7).

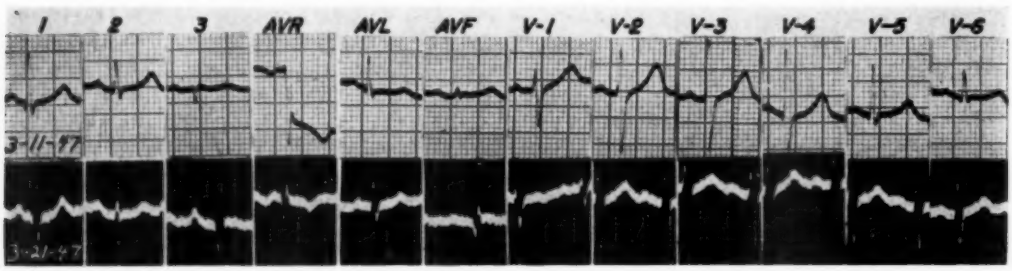

Fig. 7.—Case 7. Acute cor pulmonale due to massive atelectasis in a 56-year-old man with renal stones.

Upper tracing: **Normal preoperative electrocardiogram.** ***Lower tracing:*** **Taken following collapse and dyspnea on second postoperative day. This shows development of prominent S_1 and Q_3, lowering of T_2 and inversion of T_3. Unipolar limb leads show a prominent Q wave in aV_F. Chest leads show inversion of the T wave in V_1 and shift of transitional zone to V_6, strong confirmatory evidence for acute cor pulmonale despite a prominent Q wave in aV_F. The patient died three days later. Autopsy showed massive atelectasis of both lungs. The heart was normal except for slight hypertrophy.**

The patient died three days later. Post-mortem examination showed complete atelectasis of the lower lobes and partial atelectasis of the other lobes of both lungs due to aspiration of gastric contents. The heart was normal except for slight hypertrophy.

The changes in the conventional leads were suggestive, and the inversion of the T wave in V_1 and the shift of the transitional zone to the left were strong confirmatory evidence of acute cor pulmonale. A relatively prominent Q wave[12,13] and inverted T wave developed in aV_F but posterior myocardial infarction was not found.

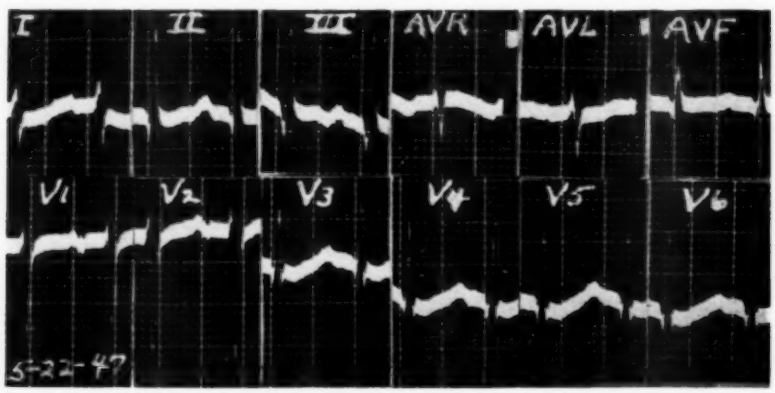

Fig. 8.—Case 8. Posterior myocardial infarct simulating acute cor pulmonale in a 72-year-old woman in coma.

Electrocardiogram shows deep S_1, depressed ST_1, inverted T_3 and presence of a Q_2 and Q_3. Unipolar limb leads show a small Q wave in aV_F measuring 0.03 second in duration. Chest leads show slight depression of the RS-T segment in V_3 through V_6. Diagnosis of acute cor pulmonale was favored over posterior myocardial infarct because of the small Q wave in aV_F. The patient died six days later. Autopsy showed posterior myocardial infarct about one week old.

CASE 8 (P.B.B.H., 6A36).—F.M., a 72-year-old housewife, was admitted to the hospital on May 18, 1948 in coma and shock. An electrocardiogram showed a prominent S_1, depressed RS-T_1 and RS-T_2, prominent Q_2 and Q_3, low T_2, and biphasic T_3. The RS-T segment in aV_L was slightly depressed. A small Q wave in aV_F was present. The unipolar chest leads were not remarkable except for slight depression of the RS-T segments in V_3 through V_6 (Fig. 8). Because of the small size of the Q wave in Lead aV_F it was considered more likely that the patient had acute cor pulmonale than posterior myocardial infarction.[10] Unfortunately there were no previous or subsequent electrocardiograms for comparison.

The patient died six days later without regaining consciousness. Autopsy showed a posteroseptal myocardial infarct approximately one week old. There were no pulmonary infarcts or emboli.

This report emphasizes the difficulty of differentiating between posterior myocardial infarction and acute cor pulmonale on the basis of a single tracing. It also demonstrates that a small Q wave may be present in Lead aV_F in posterior infarction. Several clues might have militated against the diagnosis of acute cor pulmonale. These were the position of the transitional zone between V_2 and V_3, the upright T waves over the right ventricle, and the absence of an R′ in a V_R.

DISCUSSION

When it was first appreciated that certain electrocardiographic changes may develop in acute cor pulmonale, the three standard limb leads and a single bipolar chest lead were in current use. It was recognized at the very outset[2] that the T wave in the chest lead might be reversed in direction. Subsequent experience has taught that this T-wave inversion is noted over the right ventricle[4,6,7] and that it may be accompanied by a shift of the transitional zone toward the left. This shift accounts for the presence of a right ventricular potential at points where left ventricular potentials are usually noted.

The S wave which develops in Lead I may in some instances be the effect of potential changes at the right and left shoulders, singly or in combination. Since a late R or R′ wave occasionally develops (as a consequence of backward rotation of the apex of the left ventricle[10] or of dilatation of the pulmonary conus) at the right shoulder (aV_R), and since the polarity of the potentials at the right shoulder is reversed in Lead I, the late upright deflection in aV_R becomes an S wave in Lead I. At the same time, because of the shift of the septum toward the left (apparently due to dilatation of the right ventricle which rotates the heart clockwise on its long axis[7]), the potential at the left side of the precordium and at the left shoulder may develop or accentuate an S wave. The polarity of the left shoulder remains unchanged in Lead I, hence this S wave in aV_L may contribute to S_1. Thus the development of an S_1 in acute cor pulmonale, in some patients, appears to be due to a change in the electrical position of the heart.

Similarly the Q_3 may sometimes be explained as the result of the R wave at the left shoulder (aV_L), entering into the formation of bipolar Lead III in a negative manner, algebraically added to a small septal Q wave in aV_F. The cause of the T-wave changes is not so clear. It is well known that T-wave changes in the precordial leads in anterior myocardial infarction may not be reflected in the limb leads. This is particularly true in anteroseptal infarction.

By the same token it is conceivable that T-wave changes due to acute cor pulmonale may be restricted to certain precordial leads. In instances with no rotation of the heart, QRS changes would not appear in the limb leads and T-wave changes in certain precordial leads might be the only finding. Case 3 is an example of this. And as in the instance of myocardial infarction, it is conceivable that precordial leads may show decisive changes while standard leads show equivocal changes (Cases 4, 5, and possibly 1, 6, and 7).

On theoretical grounds, unipolar rather than bipolar chest leads are preferable in the diagnosis of acute cor pulmonale. As stated above, an important criterion for this diagnosis is a shift of the transitional zone to the left. If CF leads are taken, the precordial leads, particularly on the left side, are distorted because of the high potential of the left leg which is often noted in these patients. The electrical effect of the left leg potential, which has a reversed polarity in CF leads, is to produce an absolute or relative decrease in the height of the R wave and thus to give an impression of apparent leftward displacement of the transitional zone.[14]

In either posterior myocardial infarction or acute cor pulmonale the electrocardiogram may show a deep S_1, deep Q_3, inverted T_3, depressed RS-T_1, and elevated RS-T_3. Because of the difficulty in differentiating these conditions electrocardiographers have hoped that the use of the unipolar limb leads might give decisive information on this problem. Goldberger[10] was of this opinion, stating that "the unipolar extremity leads enable the differentiation to be easily made because the left leg lead does not show an abnormal Q wave in a case of pulmonary embolism even when Q_3 is very deep, whereas it shows a typical abnormal Q wave in a case of posterior infarction." In Cases 2 and 7 an abnormal Q was present in aV_F yet the patients did not have posterior myocardial infarction. Furthermore in a parallel study[1] of eighteen acute posterior myocardial infarctions, three patients showed no abnormal Q wave in aV_F. Case 8 is one such patient.

The present experience suggests that the full set of precordial leads is most valuable in this difficult differential diagnostic problem. In posterior infarction the precordial T wave is either normally upright or extremely tall. In acute cor pulmonale, on the other hand, the T wave is apt to be inverted over a greater or lesser area of the precordium.

There is an increasing body of opinion which holds that acute cor pulmonale can result from small as well as large pulmonary emboli. Reflex spasm of the pulmonary arterial tree can be induced by small emboli and result in acute pulmonary hypertension.[15] The clinical counterpart of this phenomenon is exemplified in two patients (Cases 2 and 3) who developed electrocardiographic changes in acute cor pulmonale following single small-vessel embolization with small pulmonary infarcts.

That acute cor pulmonale may be due to causes other than pulmonary embolism is illustrated in one patient (Case 7) in whom characteristic electrocardiographic changes followed massive atelectasis of both lungs. So far as we know this is the first such instance reported. It seems reasonable that

other conditions capable of producing acute pulmonary hypertension may also be associated with this electrocardiographic picture.

In most patients in this series, the time interval between the onset of the acute episode and the recording of the electrocardiogram was very short, usually within an hour. The changes of acute cor pulmonale had developed in this short interval in five patients (Cases 1, 2, 5, 6, and 7). In one patient, however, no change was shown until the following day (Case 3). One patient showed a return of the electrocardiogram to its original form six days after the pulmonary embolism (Case 4). Another patient who had repeated pulmonary infarcts showed persistent electrocardiographic changes during seven weeks of hospitalization (Case 1).

The medical profession has become increasingly aware of the frequency of acute cor pulmonale particularly following surgery and in patients with congestive heart failure. It has been felt that the electrocardiogram is of value in establishing this diagnosis in only a relatively small percentage of patients.[4,16] It is our feeling that the diagnosis will be made more frequently and accurately if: (1) clinicians develop an even higher index of suspicion and obtain electrocardiograms when any untoward symptoms develop in a postoperative patient, cardiac, or other bedridden patient, and (2) frequent, serial unipolar, limb, and chest leads are taken in such patients.

SUMMARY

The electrocardiographic diagnosis of acute cor pulmonale was made in eight and favored in a ninth patient studied with standard and unipolar limb and chest leads and subsequently examined post mortem. In seven of these the diagnosis was confirmed pathologically. In this group the diagnosis could often be made on the basis of changes in the standard leads.

The precordial leads frequently gave corroborative and occasionally decisive evidence for the diagnosis, the evidence consisting of inversion of T waves in one or more precordial leads, shift of the transitional zone to the left, and corroborative evidence of incomplete right bundle branch block. Unipolar limb leads were not apt to be so helpful. In two patients an abnormal Q wave was present in the unipolar left leg lead (aV_F). In these patients acute pulmonary embolism and not posterior myocardial infarction was found at autopsy. In our eighth patient the diagnosis of acute cor pulmonale was favored over posterior myocardial infarction because of an inconspicuous Q wave in aV_F but autopsy showed an acute posterior myocardial infarct and no pulmonary embolism. One instance of acute cor pulmonale was associated not with pulmonary embolism but with massive pulmonary atelectasis.

The electrocardiogram may give the first clue to the diagnosis of acute cor pulmonale. This electrocardiographic diagnosis can be made with a high degree of accuracy.

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THE ELECTROCARDIOGRAPHIC SIGNS OF MYOCARDIAL INFARCTION IN THE PRESENCE OF BUNDLE BRANCH BLOCK

I. MYOCARDIAL INFARCTION WITH LEFT BUNDLE BRANCH BLOCK

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THE combination of myocardial infarction and bundle branch block is not uncommon.[1] In a large series of cases of coronary occlusion studied by Master and his associates,[2] it was present in 15 per cent of the cases. Many observers[1-5] have stressed the difficulty of recognizing the electrocardiographic evidence of myocardial infarction when bundle branch block is present. There was a time when the diagnostic difficulty was so great that single cases of bundle branch block with signs of myocardial infarction were considered worth reporting.[6,7] In recent years considerable progress in the diagnosis of myocardial infarction with bundle branch block resulted from the experimental work of Wilson and associates.[8-10] These investigators showed that changes in the QRS complex diagnostic of myocardial infarction are readily observed in the presence of right bundle branch block but are ordinarily absent when the left branch is affected. They held that changes of the RS-T segment and T wave may then be suggestive of myocardial infarction when the area of the QRS complex is small.

In spite of these diagnostic advances, uncertainty still seems to prevail among clinicians as to which features of the electrocardiogram are due to bundle branch block and which should be attributed to myocardial infarction. Changes in the chest leads, common in left bundle branch block, have been attributed to infarction of the right ventricle.[11] The possibility of diagnosing posterior infarction in the presence of right bundle branch block has been questioned[12] although Rosenbaum and associates[9] have pointed out that a disturbance of conduction in the right division of the bundle does not obscure the signs of posterior infarction which appear in the limb leads. So far only a small number of clinical cases of right bundle branch block, and still fewer instances of left bundle branch block, have been reported which presented electrocardiographic signs of myocardial infarction.[1,13,14]

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The following study was undertaken in an effort to differentiate the features of "pure"* left bundle branch block from superimposed changes due to myocardial infarction. Especial attention was given to the changes of the RS-T segment and the T wave. The study includes twenty-eight patients with what appeared to be uncomplicated left bundle branch block and fifteen patients for whom the diagnosis was made of myocardial infarction in addition to block in the left division of the bundle.† The number of patients with uncomplicated left bundle branch block available for our study is small because an effort was made to exclude not only patients with a history suggestive of myocardial infarction but also those in which there was complaint at any time of anginal pain in conjunction with either effort or rest. It has been repeatedly stressed that myocardial infarction sometimes occurs in the absence of a history of a classical coronary attack, and that it may be indicated merely by short spells of angina of effort or of rest.[1,15] By excluding patients with angina pectoris, it was expected to obtain a dependable group of patients who were suitable for comparison in as much as they presented the signs of "pure" left bundle branch block. We realize that the value of such a small group for statistical purposes is limited.

In the patients with "complicated" left bundle branch block, the diagnosis of myocardial infarction was based on: 1) post-mortem findings; 2) evidence of infarction shown by tracings which either preceded the development of bundle branch block or were taken after disappearance of bundle branch block; and 3) the classical clinical picture and confirmatory laboratory evidence of myocardial infarction.

1. THE ELECTROCARDIOGRAPHIC FEATURES OF UNCOMPLICATED LEFT BUNDLE BRANCH BLOCK

The changes of the QRS complex in experimental left bundle branch block, which resemble closely those seen in human left bundle branch block, were described by Wilson and his group.[8,10] In the tracings of man (Figs. 1 and 2) the standard limb leads show, in addition to prolongation of the QRS complex to 0.12 second or more, a monophasic initial ventricular complex in Lead I that is upright, broad, slurred, and often bifid. Q and S deflections are extremely rare in Lead I when left bundle branch block is uncomplicated. Chest leads from the right side reveal a small R and a deep, broad S deflection; occasionally the R deflections are absent. In precordial leads from left-side positions, the initial ventricular group is usually represented, as in Lead I, by a broad, slurred, and often notched, upward deflection.

Wilson and his associates employed unipolar chest leads. Their tracings do not conspicuously differ from the records we obtained from patients with left bundle branch block where we used CR or CF leads. In each of our patients

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*The terms "pure" and "uncomplicated" left bundle branch block are used here in the sense that there was neither a suspicious history nor any other evidence suggestive of myocardial infarction. We realize that in the majority of patients bundle branch block is due to coronary arteriosclerosis and is the result of an ischemic lesion interrupting the continuity of the intraventricular conduction pathways.

†Since this paper was submitted for publication seven more patients with left bundle branch block complicated by myocardial infarction were observed.

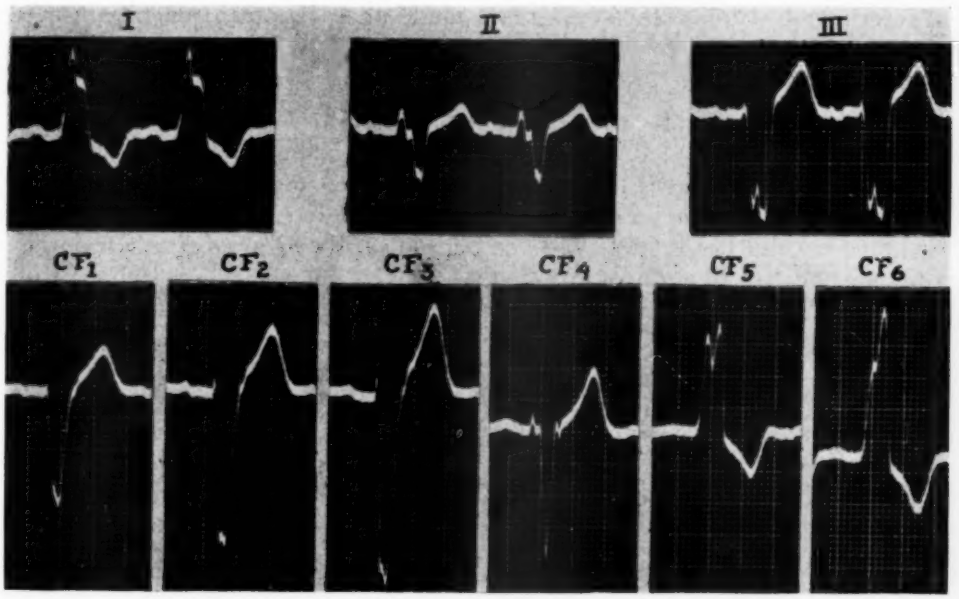

Fig. 1.—The duration of the QRS complex is 0.19 seconds. Lead I shows a broad, bifid R deflection without Q or S waves; the RS-T junction is depressed, and the T wave is inverted and of asymmetrical shape. Lead CF_5 and CF_6 resemble Lead I. In Leads CF_1 through CF_3 a low R deflection is followed by a broad, deep S wave which is notched in the apical portion; the RS-T junction is elevated and the T wave is upright. In Lead CF_3 the elevation of the RS-T segment measures 4.5 mm., and the amplitude of the T wave is 13 millimeters. Lead CF_4 presents a transitional stage between the right-side and left-side precordial patterns. The tracing shows uncomplicated left bundle branch block.

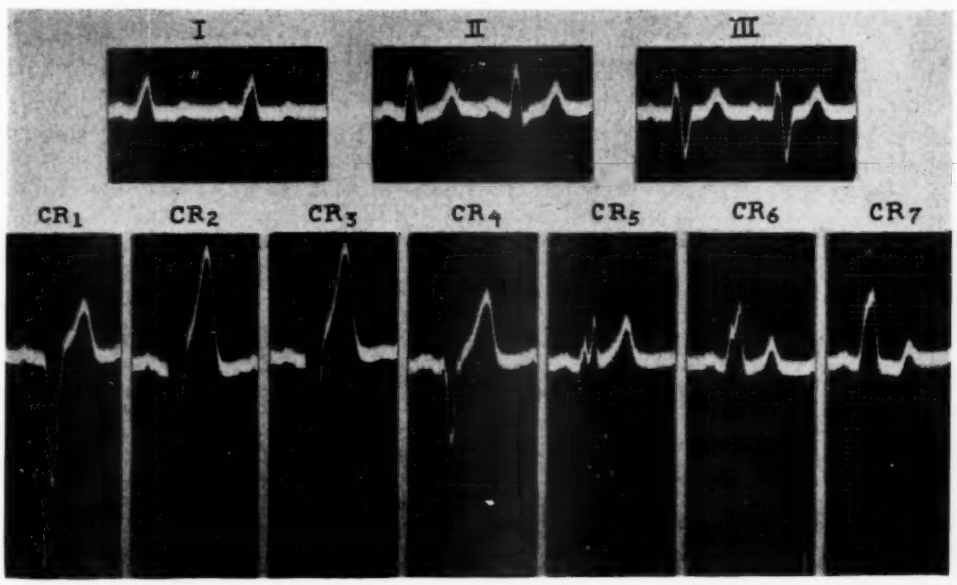

Fig. 2.—The duration of the QRS complex is 0.12 seconds. Lead I shows a broad, slurred R deflection that is not accompanied by a Q or S wave; the RS-T junction is slightly depressed and the T wave is upright. A similar shape of the ventricular complex is noted in Leads CR_6 and CR_7. Leads CR_1 and CR_2 display QS deflections with elevated RS-T junctions and high T waves. In Lead CR_2 the elevation of the RS-T segment measures close to 6 mm. and the amplitude of the T wave is 19 millimeters. Lead CR_4 presents a transitional state between the right-side and left-side precordial patterns. The tracing shows uncomplicated left bundle branch block.

at least four precordial leads were taken, and in the majority from six to seven chest leads were available. In sixteen patients CR leads were used, and, in twelve CF leads.

Table I shows the incidence of certain features of the QRS complex in uncomplicated left bundle branch block which are of significance in the differential diagnosis of superimposed myocardial infarction. Q waves were not observed in Lead I but were present three times in Lead III associated with an R deflection, and once in Lead CF_5. The amplitude of the Q waves was less than 1.0 mm. and less than one-fourth the size of the following R deflection; their duration was no longer than 0.03 second. No notching of the Q wave was observed in "pure" left bundle branch block.

TABLE I. FEATURES OF THE QRS COMPLEX, OBSERVED IN 28 PATIENTS WITH UNCOMPLICATED LEFT BUNDLE BRANCH BLOCK, WHICH ARE SIGNIFICANT IN THE DIAGNOSIS OF COMPLICATING MYOCARDIAL INFARCTION

LEAD:	I	II	III	C_1	C_2	C_3	C_4	C_5	C_6
Q waves present in:*	0	0	3	0	0	0	0	1	0
R waves absent (QS deflections) in:	0	0	7	13	8	5	1	0	0
R deflections less than 1.0 mm. high in:	0	0	5	8	5	3	4	0	0

*The figures refer to the number of patients.

R deflections were frequently absent or measured less than 1.0 mm. in Lead III or in leads from the right side of the precordium (Fig. 2). QS deflections or prominent S waves that occurred in leads from the right side of the precordium often showed conspicuous slurring or notching (Fig. 1); the notch was usually close to the apical portion, resulting in a W-shaped QS complex. No marked notching was observed in the upper two-thirds of the descending limb of deep S or QS deflections.

As has been mentioned, particular attention was given to the features of the final ventricular complex, because abnormalities of the RS-T segment and the T wave are of paramount importance in the diagnosis of myocardial infarction complicating bundle branch block, especially when changes of the QRS complex are absent or of equivocal meaning. In bundle branch block the initial and final ventricular complexes tend to move in opposite direction, the more as the amplitude of the QRS complex becomes larger. Table II shows the relationship of the initial and final ventricular groups in those leads where the main QRS deflection was upright. Prominent R deflections were invariably present in Lead I and in the precordial lead from the C_6 position. They were usually associated with depressed RS-T junctions. Only in two instances was the RS-T junction isoelectric in Lead I, and in one instance in the precordial lead taken from Position C_6. In general, depression of the RS-T junction increased with the amplitude of the R wave. The depression measured, in Lead I, a maximum

of one-seventh of the amplitude of the preceding R deflection while in leads from the left side of the chest the maximum measurement was one-eighth of the amplitude of the R wave. In Lead I and in the precordial lead from Position C_6, prominent R deflections were never associated with elevated RS-T junctions. High R deflections were only three times followed by elevated RS-T junctions; this happened in the precordial leads from Positions C_4 and C_5 which represented a transitional phase between the typical precordial patterns from the right side and left side.

TABLE II. PROMINENT R DEFLECTIONS AND THEIR RELATIONSHIP TO POSITION OF THE RS-T SEGMENT AND DIRECTION OF THE T WAVE IN 28 PATIENTS WITH UNCOMPLICATED LEFT BUNDLE BRANCH BLOCK

LEAD:	I	II	III	C_1	C_2	C_3	C_4	C_5	C_6
Prominent R deflections present in:*	28	14	3	0	0	0	7	21	23†
Prominent R deflections with depressed RS-T junctions in:	26	12	2	0	0	0	4	14	22
Prominent R deflections with isoelectric RS-T junctions in:	2	2	1	0	0	0	2	5	1
Prominent R deflections with elevated RS-T junctions in:	0	0	0	0	0	0	1	2	0
Prominent R deflections with inverted or mainly inverted (∓) T waves in:	17	3	1	0	0	0	1	11	14

*The figures refer to the number of patients.

†Lead C_6 was not available in five instances; in these instances a prominent R wave was present in Lead C_5.

Inversion of the T wave was less regularly associated with prominent R deflections than was depression of the RS-T junction. Inverted or mainly inverted (minus-plus) T waves were present in Lead I in seventeen instances and in the precordial lead from position C_6 in 14 instances (Table II, bottom line). In the other instances, prominent R deflections were accompanied by either upright or slightly diphasic (minus-plus) T waves. The inverted or mainly inverted T waves were always of asymmetrical shape, their ascending limb pursuing a steeper course than the descending limb. Their RS-T junction was depressed in all but three instances; in the latter it was at the isoelectric line.

Table III shows the incidence of prominent S waves in various leads in relation to the position of the RS-T junction and direction of the T waves. Prominent S waves were invariably present in the precordial leads from Positions C_1 and C_2, and in the majority of instances in Lead III and in the precordial leads from Positions C_3 and C_4. They were infrequently observed in Lead II and in the precordial lead from Position C_5, and never occurred in Lead I and in the precordial lead from Position C_6. Prominent S waves were usually associated with elevated RS-T junctions and upright T waves. Lead III was an exception; the RS-T junction was, in two instances, isoelectric, and in two slightly depressed; the T wave was once diphasic (minus-plus) and once inverted.

TABLE III. PROMINENT S DEFLECTIONS AND THEIR RELATIONSHIP TO POSITION OF THE RS-T JUNCTION AND DIRECTION OF THE T WAVE IN 28 PATIENTS WITH UNCOMPLICATED LEFT BUNDLE BRANCH BLOCK

LEAD:	I	II	III	C_1	C_2	C_3	C_4	C_5	C_6
Prominent S deflections present in:*	0	7	23	27†	27‡	25	18	1	0
Prominent S deflections with elevated RS-T junctions in:	0	7	19	27	27	25	18	1	0
Prominent S deflections with upright T waves in:	0	7	21	27	27	25	18	1	0

*The figures refer to the number of patients.
†Lead C_1 was not available in one instance.
‡Lead C_2 was not available in one instance.

Upward displacement of the RS-T junction and height of the T wave were often of remarkable size in those leads from the right side of the precordium which showed the largest amplitude of the S wave, usually in the precordial leads from Positions C_2 and C_3 (Figs. 1 and 2). Elevation of the RS-T junction measured from 5.0 to 6.0 mm. in seven instances and in one, even 7.0 millimeters. Upright T waves with an amplitude ranging from 10 to 19 mm. were observed sixteen times. When the RS-T junction was elevated, it was followed by an upright T wave whose amplitude equaled at least twice the distance of the elevated RS-T junction from the baseline.* Only three times in 120 instances of elevation of the RS-T junction observed in various leads, was the amplitude of T slightly less. In no case was an elevated RS-T junction followed by a flat, diphasic (plus-minus), or inverted T wave.

Table IV records the data concerning the features of the final ventricular complex in Leads II and III. The T wave was upright in Leads II and III in the majority of the tracings. Inverted or mainly inverted (minus-plus) T waves were observed five times in Lead II and four times in Lead III. In two instances the T wave was inverted in Leads II and III. The depth of the inverted T waves was invariably less than 3.0 millimeters. The shape of the inverted T waves was asymmetrical; only once did Lead III show inverted T waves with symmetrical limbs. The RS-T junction was elevated in Lead II in seven instances, in Lead III, in eighteen, invariably in association with a prominent S deflection. Elevation of the RS-T junction was, as a rule, proportionate to the amplitude of the preceding S deflection; in Lead II it measured a maximum of one-sixth of the amplitude of the S deflection in the same lead, and in Lead III a maximum of one-seventh of that amplitude.

Diphasic T waves of the plus-minus or "coronary" type were usually not observed in Leads II and III; nor were they present in the other leads except in one tracing which showed diphasic (plus-minus) T waves in Leads CR_2 and CR_3. In that particular tracing it was doubtful whether the inverted phase was part of the T wave or was caused by an inverted U wave. The same tracing showed an inverted T wave of "coronary" type in the transitional zone (Lead CR_4).

*This relationship did not hold true for patients with digitalis effect.

TABLE IV. THE FINAL VENTRICULAR COMPLEX IN LEADS II AND III IN TWENTY-EIGHT PATIENTS WITH UNCOMPLICATED LEFT BUNDLE BRANCH BLOCK

LEAD:	II	III
Upright T waves present in:*	19	22
Inverted or mainly inverted (∓) T waves in:	5	4
Diphasic (∓) T waves with shallow inverted phase in:	4	2
Diphasic (±) T waves in:	0	0
RS-T junction elevated in:	7	18
RS-T junction depressed in:	11	6
RS-T junction isoelectric in:	10	4

*The figures refer to the number of patients.

2. ANTERIOR WALL INFARCTION WITH LEFT BUNDLE BRANCH BLOCK

Our study includes ten patients with left bundle branch block in which the diagnosis of anterior infarction was made; one patient also presented signs of posterior infarction. In two, anterior infarction was shown to be present by post-mortem examination. In a third, the diagnosis of infarction was confirmed by significant findings in tracings which were obtained after disappearance of the bundle branch block pattern. In two others serial tracings showed progressive changes which suggested recent anterior infarction. In the remaining five patients the diagnosis of infarction was based on significant clinical and laboratory findings.

CASE REPORTS

CASE 1.—E. F. was a 63-year-old woman. On Dec. 11, 1945 she was seized with terrific pain in the chest which lasted for several hours.

An electrocardiogram (Fig. 3) was taken one day after the attack. In addition to the pattern of left bundle branch block, it shows features which are suggestive of anterior infarction. In Lead I a Q deflection is present and the RS-T junction is slightly elevated and followed by an inverted, shallow T wave of symmetrical shape. A QS deflection is observed in Lead CR_4, and Q waves are present in Leads CR_5 and CR_6. In the leads from the right side of the precordium, elevation of the RS-T junction is unusually marked, measuring from 9 to 13 mm. and it is followed by a rapid downstroke instead of a high T wave. In Lead CR_5 a prominent R deflection is associated with abnormal elevation of the RS-T junction. Note the presence of R deflections in Leads CR_1 and CR_2.

The patient died one week after the coronary attack. Post-morten examination revealed a recent myocardial infarction which involved the whole length of the interventricular septum. It was most marked anteriorly and extended a distance of 0.5 cm. over the anterior wall of the left ventricle adjoining the septum.

Summary: In the presence of left bundle branch block, anterior wall infarction was indicated by changes of the QRS complex in Leads I, CR_5, and CR_6, and by significant elevation of the RS-T junction in Leads I and CR_1 through CR_5. Post-mortem examination showed anterior infarction with extensive involvement of the interventricular septum.

CASE 2.—B. S. was a 60-year-old man. He was admitted to the hospital, unconscious, on Feb. 24, 1947, no history could be obtained, and he died on March 2, 1947. A post-mortem examination was not obtained.

The first electrocardiogram (Fig. 4, *A*) was taken on Feb. 28, 1947. It shows auricular flutter and signs suggestive of left bundle branch block. The latter, however, is inconstant as shown in Lead II. Some features do not fit the pattern of left bundle branch block and indicate anterior infarction. Broad, slurred, or notched Q waves are present in Leads I, CF_5, and CF_6. In Lead I the RS-T junction is elevated and followed by an inverted T wave of rather symmetrical

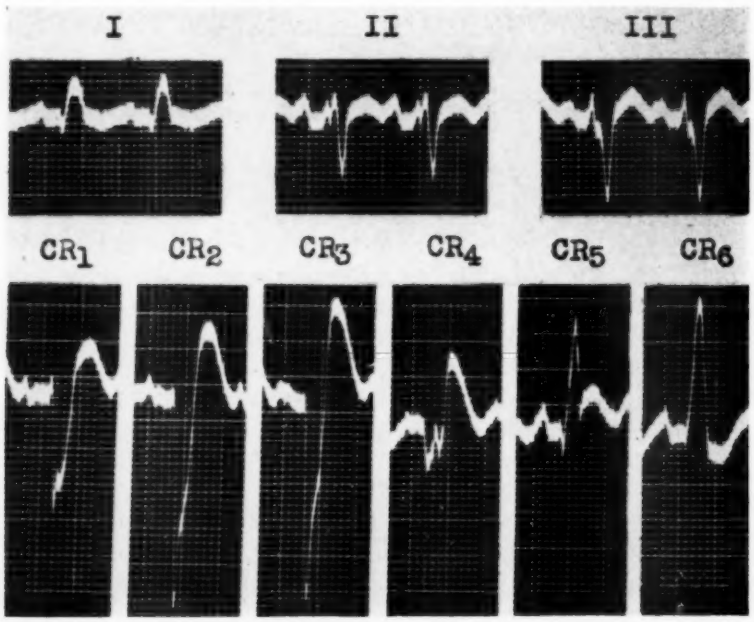

Fig. 3 (Case 1).—The tracing, taken one day after the coronary attack, shows, in addition to the pattern of left bundle branch block, signs suggestive of anterior infarction. These are: Q waves in Leads I, CR_5, and CR_6; in the chest leads significant elevation of the RS-T junctions not followed (as in uncomplicated left bundle branch block) by high peaked T waves. In Lead CR_3 elevation of the RS-T junction measures 13 mm.. R waves are present in Leads CR_1 and CR_2. Post-mortem examination showed anterior infarction mainly involving the interventricular septum.

shape. Some irregularities in the shape of the QRS complex and T wave in successive beats are probably due to fusion with varying phases of flutter waves. In the leads from the left side of the chest (CF_5 and CF_6), the RS-T junction is significantly elevated and followed by an inverted phase of the T wave. The second tracing (Fig. 4, *B*) was taken four days after *A*. It displays progressive changes. Lead CF_4 shows sudden decrease of the height of the R wave while Lead CF_5 shows a Q wave of marked amplitude. Elevation of the RS-T junction in the leads from the left side of the chest is diminished. Inversion of the T wave is more pronounced in Leads I and CF_6.

Summary: In the presence of left bundle branch block, the electrocardiogram showed signs of anterior infarction similar to those in Case 1 (Fig. 3), namely: unusually broad and deep, slurred or notched Q waves in Leads I, CF_5, and CF_6; an inverted T_1 of symmetrical shape and with a slightly elevated RS-T junction; and significant elevation of the RS-T junction in Leads I, CF_5, and CF_6. The significant changes were progressive in subsequent records.

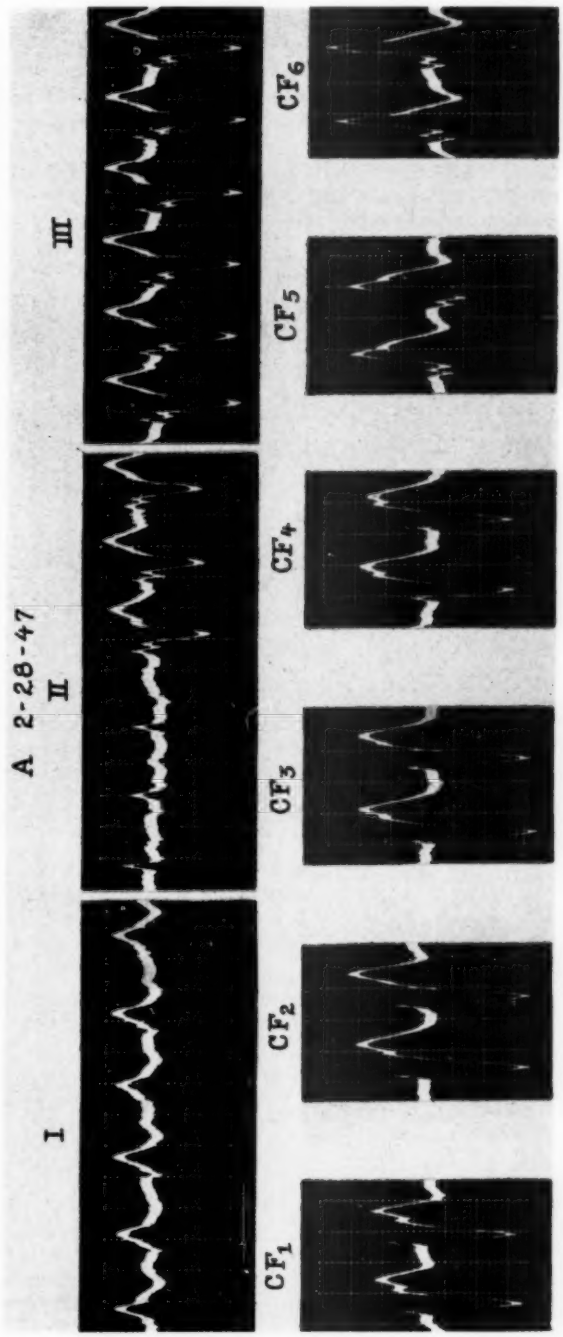

Fig. 4 (Case 2).—*A*, the tracing shows auricular flutter (Lead II) and the pattern of left bundle branch block. In Lead II the bundle branch block is inconstant. Signs suggestive of anterior infarction are: broad, notched, and slurred Q waves in Leads I, CF_5, and CF_6 and significant elevation of the RS-T junction in Leads I, CF_3 through CF_6.

CASE 3.—L. L. was a 76-year-old man. On Dec. 9, 1946 he experienced a prolonged attack of severe chest pain during which he perspired freely. The attack was followed by increase of the white blood count and sedimentation rate and by an abrupt fall in blood pressure.

The first electrocardiogram (Fig. 5, *A*) was taken on the day of the attack. It shows the pattern of left bundle branch block. An unusual feature is the presence of a small Q deflection in Leads I and CR_4 through CR_6, while low R waves are noted in Leads CR_1 and CR_2. The second tracing (Fig. 5, *B*) was taken nine days after *A*. Distinct Q waves are present in Leads I and II and the amplitude of the Q wave has markedly increased in Leads CR_4 and CR_5. Depression of the RS-T junction which previously was marked in Leads I and CR_4 through CR_6, is greatly diminished.

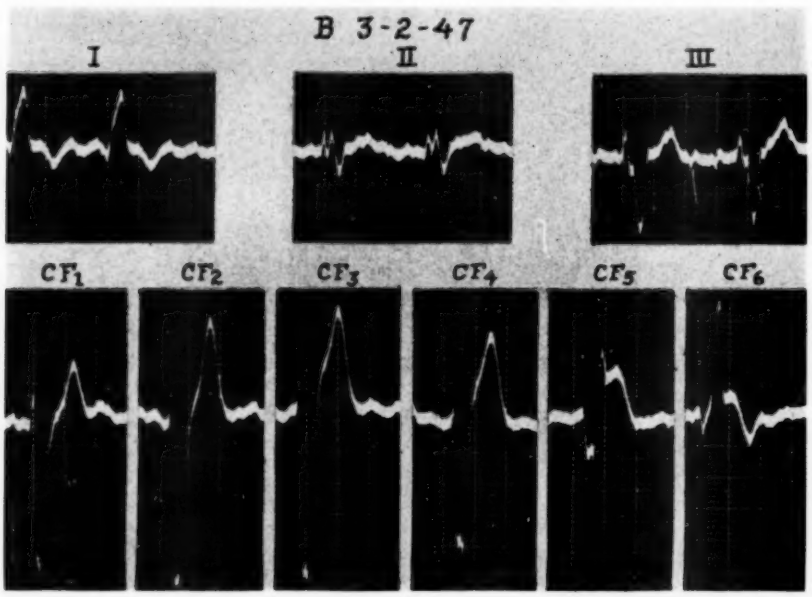

Fig. 4.—*B*, taken four days after *A*. The changes which are suggestive of anterior infarction show a progressive character. In Lead CF_5 the amplitude of the Q wave has increased. Elevation of the RS-T junction in Leads CF_4 through CF_6 is diminished. Inversion of the T wave in Leads I and CF_6 is more pronounced. Note the symmetrical shape of T_1.

Summary: Following an attack indicative of myocardial infarction, the electrocardiogram showed, in addition to the pattern of left bundle branch block, Q waves in Lead I and the leads from the left side of the chest. In successive tracings the amplitude of the Q waves increased, while depression of the RS-T junction, which was first marked in Lead I and in the leads from the left side of the chest, greatly diminished.

CASE 4.—H. L. S. was a 64-year-old man. He gave a history of coronary occlusion which had occurred four years before the electrocardiogram was taken.

The electrocardiogram (Fig. 6) shows in the limb leads a prominent R deflection, a broad, slurred Q wave, and an inverted T wave with fairly symmetrical limbs. In Leads I and II, the RS-T junction is slightly elevated. The duration of the QRS complex is 0.14 second. Lead I shows no S deflection. The chest leads present the pattern of left bundle branch block. In addition, there are features suggestive of anterior infarction. While R deflections are present in the precordial leads from the right side, Lead CF_5 shows a QS deflection. In Lead CF_6 a deep, broad, and notched Q wave precedes the late peak of the R wave, the RS-T junction is elevated, and the T wave is diphasic (plus-minus).

While the changes in the chest leads are those of anterior infarction, the presence of a Q wave in Leads II and III might suggest posterior wall involvement. Lead aV_F resembles Lead CF_6; Lead aV_L is of low voltage and like Lead aV_F shows a marked Q wave; the heart is in semivertical position.[10] This electrical position explains why the changes of anterior infarction are observed in the unipolar lead from the left leg and therefore in Leads II and III. On the other hand, the unusual finding of an R deflection in Lead aV_R contributes greatly to the development of Q waves in Leads I and II.

Summary: The chest leads indicate left bundle branch block and anterior infarction. The limb leads suggest anterior and posterior infarction because broad and slurred Q waves are present not only in Lead I but also in Leads II and III. However, the unipolar limb leads indicate that the heart is in semivertical position; this causes the changes of potential in the anterolateral

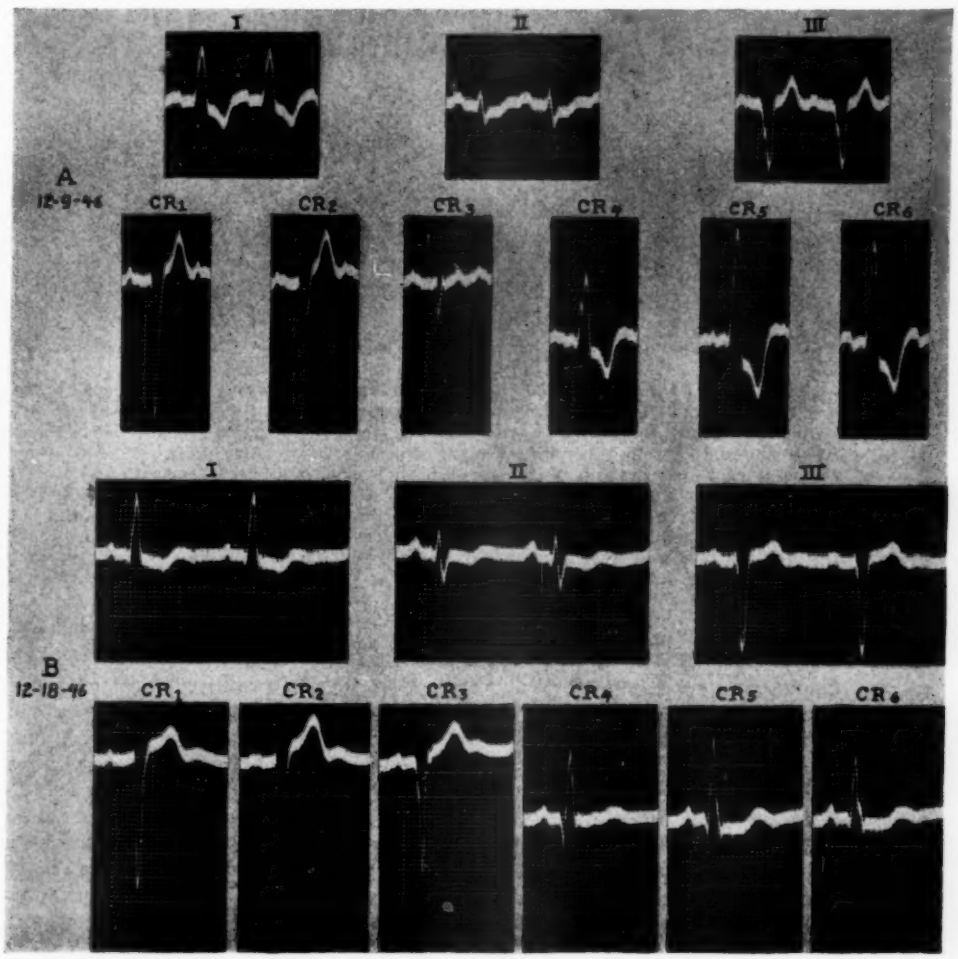

Fig. 5 (Case 3).—*A*, the tracing, taken the day of the coronary attack, shows the pattern of left bundle branch block and, as an unusual feature, small Q waves in Leads I and CR_4 through CR_6.

B, taken nine days after *A*. Distinct Q waves are present in Leads I and II. The amplitude of the Q waves has increased in Leads CR_4 through CR_6. Note the presence of R deflections in Leads CR_1 and CR_2. Depression of the RS-T segment in Leads I and CR_4 through CR_6 is less marked than previously.

wall of the left ventricle to be transmitted primarily to the left leg. Therefore, a Q wave is present in Leads II and III. Another unusual feature in the presence of left bundle branch block is the finding of an R deflection in Lead aV_R. This factor, which is probably due to marked clockwise rotation of the heart, contributes to the appearance of Q waves in Leads I and II.

CASE 5.—R. J. was a 62-year-old woman. She gave a history of a coronary attack two years previously. On Dec. 22, 1943 she experienced severe precordial pain which persisted for hours and was associated with cold sweat. The attack was followed by a rise in temperature and an increase of the sedimentation rate.

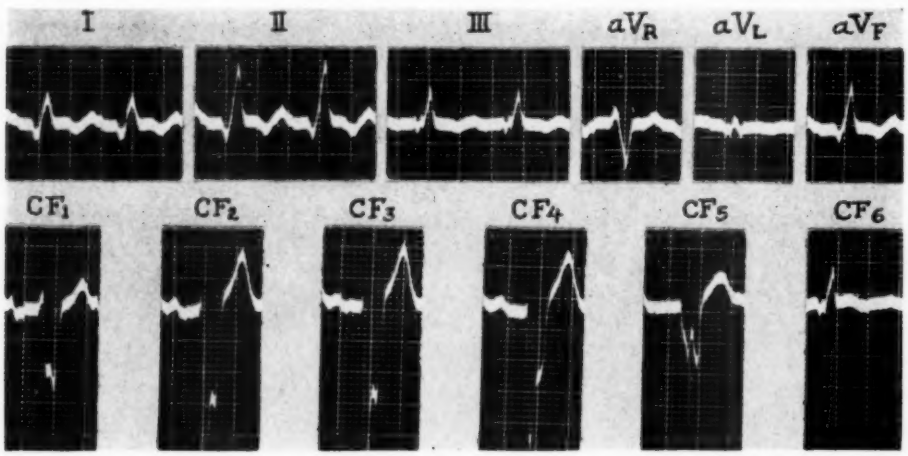

Fig. 6 (Case 4).—The chest leads indicate left bundle branch block but there are some unusual features. Lead CF_5 shows a QS deflection, while R waves are present in the precordial leads from the right side. In Lead CF_6 there is a broad, notched Q wave; the RS-T junction is slightly elevated, and the T wave is diphasic (±). These changes suggest anterior infarction. The findings of broad, slurred Q waves in all limb leads seem to indicate that, in addition, there is a posterior infarction. However, the unipolar limb leads show that these findings are due to semivertical position of the heart. Lead aV_F equals CF_6. Lead aV_L is small and shows, like the lead from the left leg, a distinct Q wave. Because of the peculiar position of the heart, Q waves, caused by anterior infarction, appear in Leads II and III. On the other hand, the unusual finding of an R deflection in Lead aV_R contributes to the appearance of Q waves in Leads I and II.

The first electrocardiogram (Fig. 7, *A*) was taken one day after the recent coronary attack. It shows the pattern of left bundle branch block and, in addition, some changes of the final ventricular complex that are suggestive of anterior infarction. T_1 is inverted with symmetrical limbs and its RS-T junction is not depressed. In Lead III the RS-T junction is markedly depressed and the T wave is high. Both the depression of the RS-T junction and the height of the T wave are out of proportion to the amplitude of the QRS complex, and represent reciprocal changes in anterior wall infarction. Leads CF_2 through CF_5 show small R deflections; the RS-T junctions are elevated and followed by plus-minus T waves. Lead CF_6 shows the same features of the RS-T junction and T wave as Lead I. The second tracing (Fig. 7, *B*) was taken eleven days after *A*. The pattern of left bundle branch block has disappeared. Changes of the final ventricular complex suggestive of anterior infarction are noted which are fairly identical with those of the previous tracing. In addition, QS deflections are observed in Leads CF_2 through CF_4, where previously a small R wave had been present. The third tracing (Fig. 7, *C*) was taken three weeks after *A*. The pattern of left bundle branch block has returned. In Leads I and III, changes of the RS-T junction and T wave, significant of anterior infarction, are no longer present, and the shape of the final ventricular complex in these leads is such as may be expected with uncomplicated left bundle branch block. Leads CF_2 and CF_4 still present changes of the T wave which are suggestive of anterior infarction. The return of left bundle branch block has been accompanied by return of the R deflections in the chest leads.

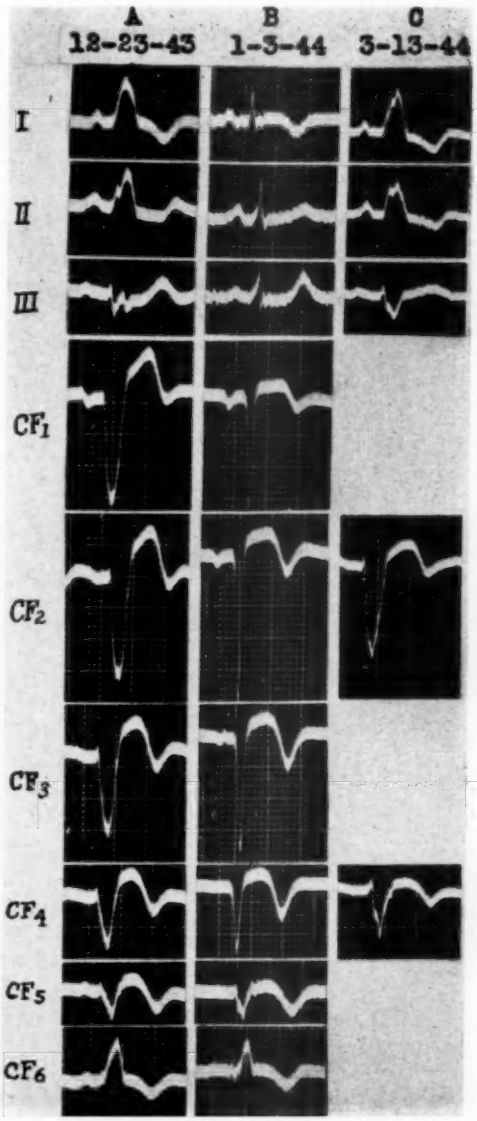

Fig. 7 (Case 5).—*A*, the tracing, taken one day after the coronary attack, shows the pattern of left bundle branch block. In addition, some changes of the RS-T segment and T wave suggest anterior infarction. T_1 is inverted and has symmetrical limbs while its RS-T junction is not depressed. Lead III shows a reciprocal depression of the RS-T segment which is out of proportion to the amplitude of S_3; T_3 is strikingly high. CF_6 resembles Lead I. In Leads CF_1 through CF_5 a deep minus deflection of the QRS complex is followed by a plus-minus T wave. Note the presence of a small R wave in Leads CF_2 through CF_5.

B, taken eleven days after *A*. The pattern of left bundle branch block has disappeared. Changes of the final ventricular complex in limb and chest leads are noted that resemble those seen in *A*. However, R waves that were previously present in Leads CF_2 through CF_4 have disappeared.

C, taken three weeks after *A*. Left bundle branch block has returned. Changes of the RS-T segment and T waves suggestive of anterior infarction are still present in the chest leads but not in the limb leads. Note depression of the RS-T segment and the asymmetrical T wave in Lead I, and slight elevation of the RS-T segment in Lead III. R deflections have returned in the chest leads.

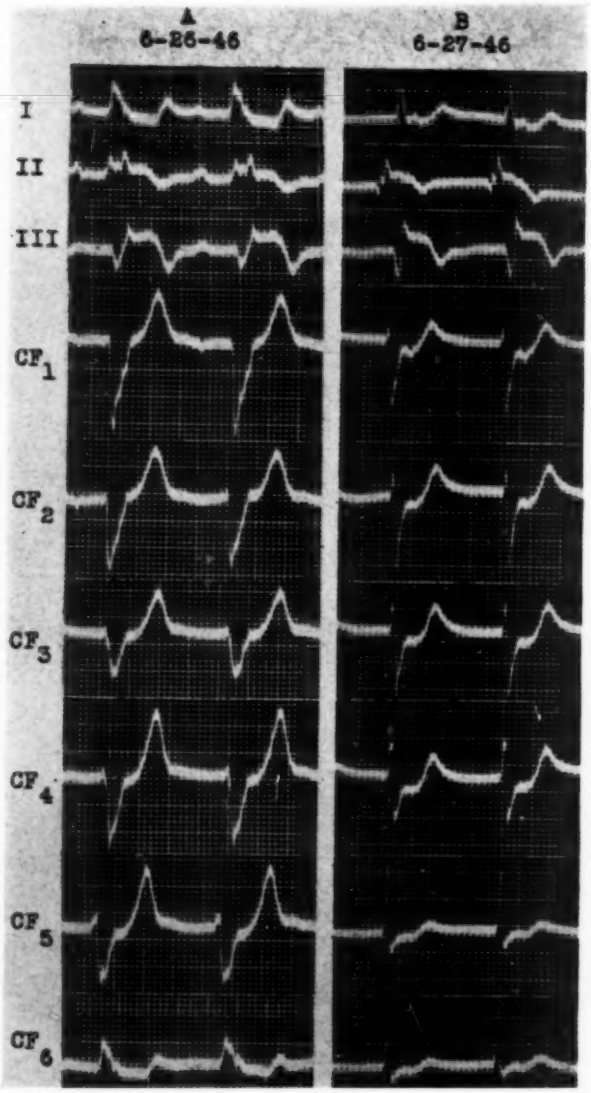

Fig. 8 (Case 6).—*A*, this tracing, taken one day after the coronary attack, shows the pattern of left bundle branch block and, in addition, signs suggestive of posterior infarction. Lead III shows a broad, slurred Q wave. No Q wave is present in Lead II. In Leads II and III there are significant elevation of the RS-T segment and inversion of the T wave. The amplitude of T_3 is more than 3 millimeters. Lead I shows a reciprocal depression of the RS-T segment which is out of proportion to the size of R_1. In the chest leads, which have a prominent S wave, the RS-T junction, instead of being elevated, is isoelectric or depressed; on the other hand, the T waves are of conspicuous height. Lead CF_6 resembles Lead I.

B, taken one day after *A*. The pattern of left bundle branch block has disappeared. Changes of the RS-T segment and T wave are similar to those in tracing *A*; besides, a significant Q wave has appeared in Lead II. In the chest leads, the T waves are lower than previously.

Post-mortem examination showed extensive recent posterior infarction.

Summary: In the presence of left bundle branch block, anterior wall infarction was suggested by significant changes of the final ventricular complex in the limb and chest leads. Similar changes were present after disappearance of the bundle branch block pattern. In addition, significant changes of the QRS complex made their appearance; these were previously masked by left bundle branch block.

3. POSTERIOR WALL INFARCTION WITH LEFT BUNDLE BRANCH BLOCK

Our study includes six patients with left bundle branch block for whom the diagnosis of posterior infarction was made; one, in whom anterior infarction was also present, has been listed already in the group of left bundle branch block with anterior infarction. In two, posterior infarction was revealed by post-mortem examination. In three the diagnosis of posterior infarction was confirmed by tracings which were obtained either prior to the development of left bundle branch block or after its disappearance. In one patient the diagnosis of posterior infarction was based on significant clinical and laboratory findings.

CASE 6.—O. K. was a 68-year-old woman. She suffered an acute coronary attack on June 25, 1946 and died on July 8, 1946.

The first electrocardiogram (Fig. 8, *A*) was taken one day after the coronary attack. It shows the pattern of left bundle branch block and also features suggestive of posterior infarction. In Lead III, a deep, broad Q wave is followed by a small R deflection. No Q wave is present in Lead II. In both Leads II and III there is significant elevation of the RS-T junction which is out of proportion to the amplitude of the QRS complex. It is followed by inversion of the T wave. The amplitude of the inverted T_3 is more than 3.0 millimeters. Lead I shows a reciprocal depression of the RS-T junction which also is out of proportion to the size of R_1. In the chest leads which display a deep S deflection, instead of the expected elevation of the RS-T junction, either an isoelectric RS-T junction is noted (CF_1 and CF_2) or marked depression of the RS-T junction (CF_3 through CF_5). Depression of the RS-T junction is associated with upright T waves of great amplitude. Lead CF_6 presents features similar to those in Lead I. The second tracing (Fig. 8, *B*) was taken one day after *A*. The signs of left bundle branch block have disappeared. Reciprocal changes of the RS-T junction and T wave in the limb leads and depression of the RS-T junction in the chest leads resemble the features of the previous tracing. There is one important difference, i. e., a Q wave has appeared in Lead II which was not present in tracing *A*. The amplitude of the T waves in the chest leads is less than in tracing *A*.

Post-mortem examination revealed extensive recent infarction involving the entire posterior wall of the left ventricle, the posterior portion of the interventricular septum, and an adjoining strip of the posterior wall of the right ventricle.

Summary: Post-mortem examination revealed an extensive, recent posterior infarction, including a portion of the interventricular septum and part of the posterior wall of the right ventricle. In the presence of left bundle branch block, posterior infarction was indicated by significant changes of the RS-T junction and T wave in the limb and chest leads. Similar changes were observed after disappearance of the bundle branch block. However, a Q wave which was noted in Lead II after disappearance of the bundle branch block, was absent in the tracing which displayed the pattern of left bundle branch block.

CASE 7.*—E. S. was a 79-year-old man. For the past six years he had complained of anginal pain associated with effort. On Sept. 16, 1942 he suffered an acute coronary attack. He died on Oct. 5, 1942.

The electrocardiogram (Fig. 9), taken on Oct. 2, 1942, shows the pattern of left bundle branch block. In addition there are features which may suggest posterior infarction. Besides a QS deflection in Lead III, a W-shaped QRS complex is noted in Lead II which, in some beats, is preceded by a tiny upstroke. We are inclined to consider this change of the QRS complex, which was unlike any we have observed in other patients with left bundle branch block, suggestive of posterior infarction. The diagnosis is confirmed by premature beats in Lead

*The case was reported in Am. J. M. Sc. **206**;361, 1943.

III which display features such as are ordinarily shown by regular beats in the presence of posterior infarction. The premature beats may be either of the "intermediate type," that is, due to excitations which activate the two ventricles in normal sequence because of suitable site of the ventricular focus; or they may possibly originate in the infarcted ventricle, causing initial negativity of potential in the cavity of that ventricle and thus allowing the development of significant Q waves in Leads II and III; or, finally, the premature beats may arise in either ventricle if it may be assumed that infarction of the interventricular septum is responsible for a negative potential at the beginning of systole in the cavities of both ventricles.[10, 16]

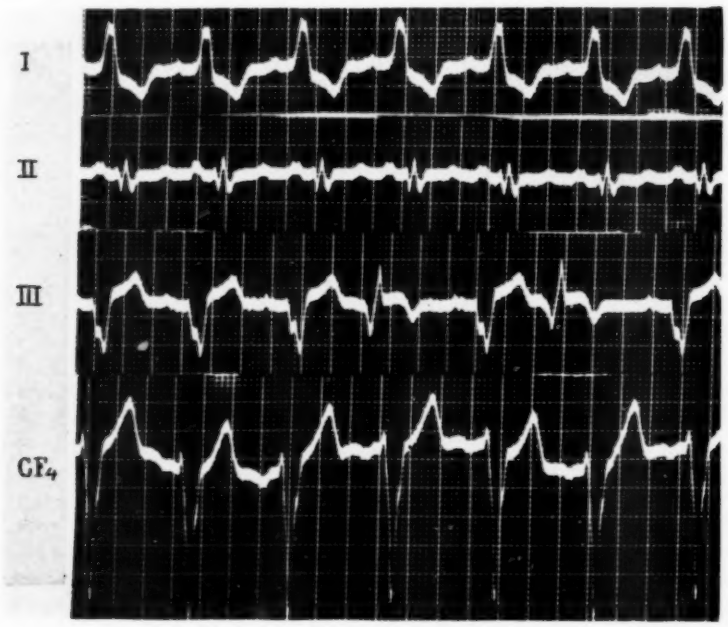

Fig. 9 (Case 7).—This tracing, taken two weeks after the coronary attack, shows the pattern of left bundle branch block. Certain features are suggestive of posterior infarction. Lead II shows a W-shaped QRS complex which, in some beats, is preceded by a tiny upstroke. In Lead III the regular beats display QS deflections; in addition, premature beats are present which are apparently of ventricular origin and show signs of posterior infarction, i.e., a deep Q deflection, elevation of the RS-T segment, and inversion of the T wave.

Post-mortem examination revealed recent infarction of the posterior portion of the interventricular septum and of the entire posterior wall of the right ventricle.

Post-mortem examination revealed an extensive recent infarction involving the posterior portion of the interventricular septum and the entire posterior wall of the right ventricle. Numerous fibrous scars were present in the anterior and posterior walls of the left ventricle.

Summary: Post-mortem examination showed recent infarction of the posterior portion of the interventricular septum and, as an unusual feature, infarction of the entire posterior wall of the right ventricle. Either of these infarcted areas might have given rise to the appearance of significant Q waves (Q wave equivalents) which are observed in Leads II and III in the presence of left bundle branch block. Posterior infarction was further indicated by the shape of the premature ventricular beats that were present in Lead III.

CASE 8.—C. N. was a 65-year-old man. He suffered a "heart attack" four years previously and was kept in bed for eight weeks. On March 16, 1947 he was awakened by pain in the right upper quadrant which gradually increased in intensity. It was thought to be due to indigestion. After the attack the heart sounds were distant and the blood pressure dropped abruptly. The patient died one day after the attack. A post-mortem examination was not obtained.

The first electrocardiogram (Fig. 10, *A*) was taken three hours after the onset of symptoms. The QRS complex is of normal duration. There are signs suggestive of acute posterior infarction. In addition, in Leads CF_1 through CF_3, R deflections are absent. This may be a residuum of the heart attack which occurred four years previously. The second tracing (Fig. 10, *B*) was taken one day after *A*. Left bundle branch block has developed. A deep and broad, notched Q wave has appeared in Lead III; and no Q wave is present in Lead II. Posterior infarction is suggested

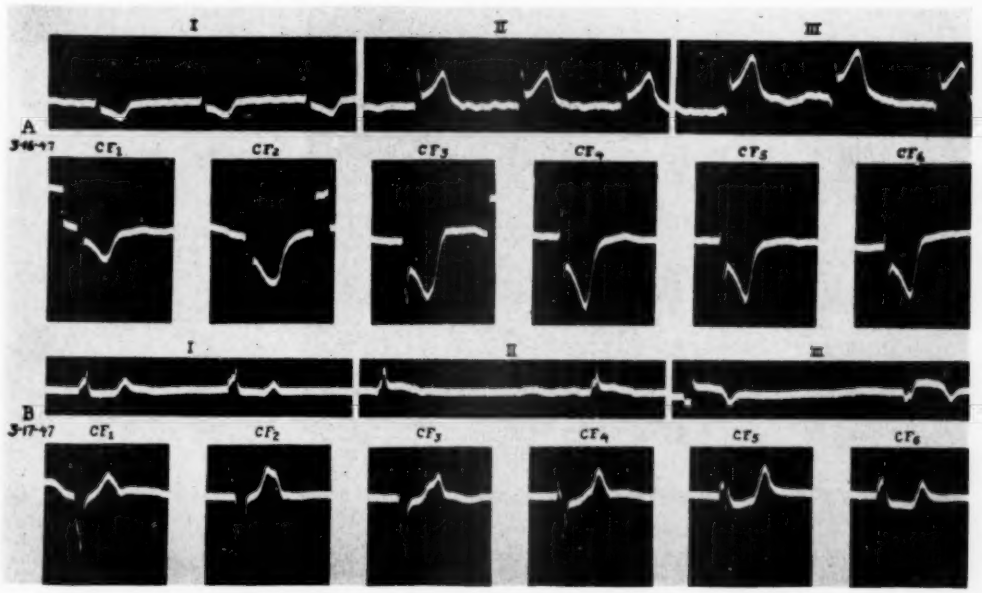

Fig. 10 (Case 8).—*A*, this tracing, taken three hours after the coronary attack, shows the signs of acute posterior infarction in limb and chest leads. The QRS complex is of normal duration.

B, taken one day after *A*. Left bundle branch block has developed. Posterior infarction is suggested in Leads II and III by marked elevation of the RS-T junction. Lead II shows terminal inversion of the T wave. T_3 is sharply inverted. Significant depression of the RS-T junction is present in all chest leads. There is a deep and broad, notched Q wave in Lead III. Q_2 is absent.

by such changes of the final ventricular complex as are not part of the left bundle branch block pattern. Leads II and III show marked elevation of the RS-T junction; it is significant in Lead II because of its association with an R deflection, and in Lead III, because the elevation of the RS-T junction is out of proportion to the size of QS_3. A terminal dip of T_2 and sharp inversion of T_3 are noted. All chest leads show depression of the RS-T junction. In Leads CF_1 through CF_4 the depression of the RS-T junction is significant by its association with deep S or QS waves, and in Leads CF_5 and CF_6 because it is out of proportion to the size of the predominant QRS deflection. As in tracing *A*, R deflections are absent in the leads from the right side of the precordium.

Summary: Acute posterior infarction was indicated by a tracing that was taken prior to the development of left bundle branch block. In the presence of left bundle branch block it was suggested by significant changes of the RS-T junction in the limb and chest leads. Q_2 was absent. A deep and broad, notched Q wave was present in Lead III.

CASE 9.—M. G. was a 68-year-old man. He suffered from diabetes. On New Year's eve of 1943, after eating and drinking to excess, he had "indigestion." He felt ill, vomited, and fainted. Afterwards the temperature rose and the blood pressure fell abruptly.

The first electrocardiogram (Fig. 11, *A*) was taken six days after the attack. It shows in the limb leads the features of arborization block and in the chest leads the pattern of left bundle branch block. In addition, there are features suggestive of posterior infarction. These are,

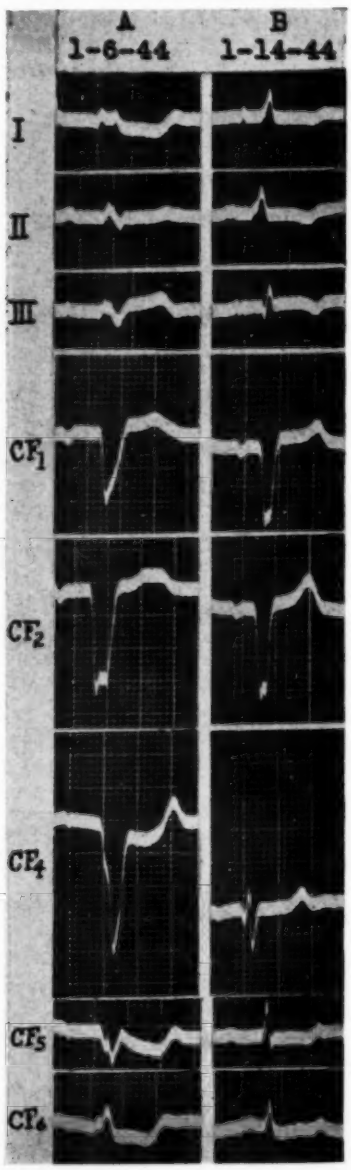

Fig. 11 (Case 9).—*A*, the tracing, taken six days after the coronary attack, shows arborization block in the limb leads and left bundle branch block in the chest leads. Some features are suggestive of posterior infarction. In Lead III the RS-T segment is elevated; in Lead I depressed. Both deviations are disproportionately large in relation to the size of the QRS complex. There is significant depression of the RS-T segment in Leads CF_4 through CF_6.

***B*, taken eight days after *A*. The pattern of left bundle branch block has disappeared but there are still signs of intraventricular conduction disturbance. A significant Q wave has developed in Lead III. "Coronary T waves" are present in Leads II and III. The chest leads show features suggestive of an anterior wall lesion, that is, QS deflections in Leads CF_1 and CF_2, and a significant Q wave in Lead CF_4.**

in Lead III, elevation of the RS-T junction, and in Lead I, depression of the RS-T segment, both disproportionately large in relation to the amplitude of the QRS complex. There is also significant depression of the RS-T junction in Leads CF_4 through CF_6. The second tracing (Fig. 11, *B*) was taken eight days after *A*. The pattern of left bundle branch block has disappeared although there are still signs of disturbed intraventricular conduction. The signs of posterior infarction in the limb leads are a significant Q wave in Lead III, and inversion of the T wave with the features of a "coronary T wave" in Leads II and III. In addition, there are other signs which point to an anterior wall lesion; namely, a QS deflection in Lead CF_2 and a significant Q wave in CF_4. Absence of the R wave in Leads CF_1, CF_2, and CF_4 was noted in tracing *A*. However, it was difficult to evaluate this sign in the presence of left bundle branch block, which may present similar features even without complicating myocardial infarction.

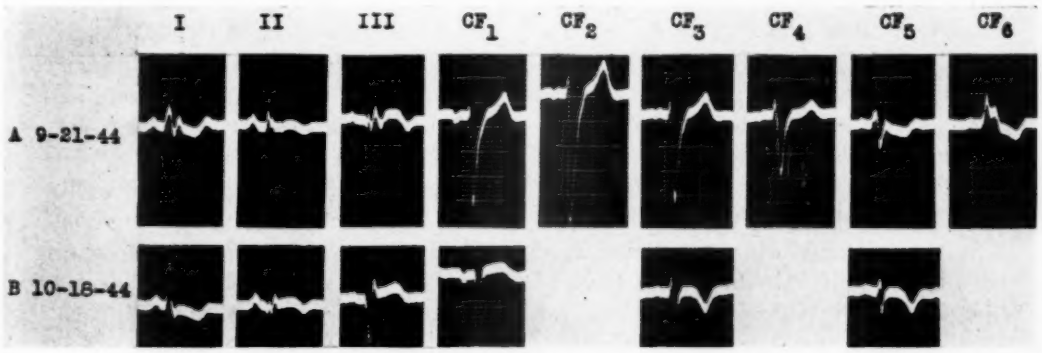

Fig. 12 (Case 10).—*A*, this tracing, taken two weeks after the coronary attack, indicatesarb orization block in the limb leads. The chest leads show the pattern of left bundle branch block. Posterior infarction is suggested by elevation of the RS-T segment in Lead III and by depression of the RS-T segment in Lead I. Both deviations are disproportionately large in relation to the amplitude of the QRS complex. Leads II and III show inverted T waves of the "Coronary type." A small Q wave is present in Lead III. Q_2 is absent.

***B*, taken four weeks after *A*. The features of left bundle branch block have disappeared. Significant Q waves are now present in Leads II and III. In addition, sharply inverted T waves have appeared in Leads CF_3 and CF_5 which were not present in the previous tracings. They point to an anterior wall lesion.**

Summary: In the presence of left bundle branch block, posterior infarction was indicated by significant reciprocal deviations of the RS-T segment in the limb leads, and by depression of the RS-T junction in Leads CF_4 through CF_6. Significant Q waves in Leads II and III were absent as long as left bundle branch block lasted. When it disappeared, a significant Q wave was observed in Lead III.

CASE 10.—R. P. was a 61-year-old woman who suffered a heart attack in 1939 and was kept in bed for three months. On Sept. 7, 1944 she experienced squeezing pain in the chest associated with cold sweat. The pain lasted for several hours. It was followed by a rise in temperature and an increase of the sedimentation rate.

The first electrocardiogram (Fig. 12, *A*) was taken two weeks after the recent coronary attack. It shows in the limb leads the features of arborization block, and in the chest leads the pattern of left bundle branch block. Some features, however, suggest posterior wall infarction: the limb leads show reciprocal deviations of the RS-T segment which are disproportionately large in relation to the size of the QRS complex; moreover, inverted T waves of the "coronary type" are present in Leads II and III; a small Q wave is observed in Lead III; and Q_2 is absent. The second tracing (Fig. 12, *B*) was taken four weeks after *A*. The features of left bundle branch block have disappeared. Significant Q waves and diphasic (plus-minus) T waves are now present in Leads II and III, confirming the diagnosis of posterior infarction. In addition, Leads CF_3 and CF_5 show sharp inversion of the T wave, suggestive of an anterior lesion that was not observed in the presence of left bundle branch block.

Summary: In the presence of left bundle branch block posterior infarction was indicated by reciprocal changes of the RS-T segment and T wave in the limb leads, and by "coronary T" waves in Leads II and III. Significant Q waves in Leads II and III did not appear until the signs of left bundle branch block had subsided. Then inverted T waves were also noted in the chest leads which may have been previously masked by left bundle branch block.

DISCUSSION

Anterior wall infarction.—Our series of myocardial infarction complicating bundle branch block includes fifteen patients with left bundle branch block and about four times this number with right bundle branch block observed during the same period of time. The rarity of left bundle branch block with infarction, which is not accounted for by different incidence of right and left bundle branch block, illustrates the difficulty in diagnosing myocardial infarction when conduction in the left division of the bundle is disturbed. Block of the left bundle branch reverses the normal sequence of activation of the ventricles. Ordinarily the left ventricle enters into activation slightly in advance of the right ventricle. Therefore the potential of the cavity of the left ventricle is negative throughout the time of activation, and chest leads from positions overlying the free wall of the left ventricle—as well as Lead I—often show a small Q deflection. In the presence of left bundle branch block, the excitation first reaches the right ventricle and spreads through the interventricular septum to the left ventricle. This causes initial positivity of potential in the cavity of the left ventricle. Hence no Q waves are, as a rule, recorded in leads from positions on the left side of the chest nor in Lead I, when left bundle branch block is present;[10,16] nor may Q waves be expected to appear in these leads when infarction occurs in the left ventricle. The occasional observation of Q waves in the presence of myocardial infarction complicating left bundle branch block has been explained by involvement of a large portion of the interventricular septum.[1,10] This reduces the magnitude of the electromotive force which is created by the spread of the excitation from the right venticle through the interventricular septum and allows the negative potential of the cavity of the right ventricle to be transmitted to the left ventricle.

In our group of twenty-eight selected patients with uncomplicated left bundle branch block, a Q wave was never present in Lead I. Sodeman and associates[16] have observed a Q_1 in eight out of ninety-two unselected patients classified as having left bundle branch block. These authors also reviewed thirty-seven instances of left bundle branch block—some of their own observation and some gathered from the literature—which presented a Q wave in Lead I. In eight of these post-mortem examination was performed; infarction of the interventricular septum was present in six. A good number of the remaining patients presented conditions that are not likely to be associated with myocardial infarction. The authors concluded that the finding of Q_1 in the presence of left bundle branch block should arouse suspicion of infarction of the interventricular septum. This factor, however, cannot be blamed—as their series of patients shows—in all instances where Q waves are found in Lead I in the presence of left bundle branch block.

In the dog, after cutting the left division of the bundle, Q_1 has been observed more often than not.[16] This was ascribed by Sodeman and associates[16] to the longitudinal orientation of the long axis of the dog's heart in the body. Because of this position the wall instead of the cavity of the right ventricle may face the attachment of the right front leg to the body and will transmit its potential, which is usually positive at the beginning of systole, to the right front leg electrode. This positive potential, in turn, may produce a negative initial deflection in Lead I, because Lead I equals $V_L - V_R$.[10] In the human being such a mechanism is not likely to occur because the heart is usually in horizontal position in the patients in whom left bundle branch block is observed, and the potential of the right arm is ordinarily negative throughout the duration of systole. Yet, in one of our patients (Case 4, Fig. 6) the unipolar limb leads indicated that the heart was in the semivertical position, and the initial ventricular complex of Lead aV_R began with a distinct upstroke. Another possible explanation for an occasional initial upstroke in the QRS complex of Lead aV_R may be that the right arm lead reflects a mixture of the negative potential of the cavity of the right ventricle with the potential of the left ventricular cavity which is positive at the beginning of systole when left bundle branch block is present.[17]

Still another mechanism was suggested by Sodeman and associates[16] as being possibly responsible for the finding of Q_1 in some infrequent instances of left bundle branch block. Abnormal congenital distribution of the conduction fibers in the right ventricle or block in some ramification of the right bundle branch may cause some part of the right ventricle other than the interventricular septum to be first reached by the excitation. Thus, at the beginning of systole, the wall of the left ventricle would face the tail of the excitation wave, and a negative initial deflection would be inscribed in precordial leads overlying the wall of the left ventricle and—presuming a horizontal position of the heart—in Lead I. If such a mechanism occurs it is extremely infrequent. Wilson and associates[10] feel so strongly about the absence of Q waves in chest leads from positions on the left side of the heart when left bundle branch block is uncomplicated, that they question the correctness of the diagnosis of left bundle branch block when Q waves are observed in these leads. Only one of our twenty-eight patients with uncomplicated left bundle branch block showed a small Q deflection in Lead CF_5 (no lead from position C_6 was available). Recently Lapin and Sprague[18] reported an instance of left bundle branch block which presented Q waves in the precordial leads from the left side, in Leads V_L and I. The Q waves became marked during inspiration and disappeared during expiration. There was no evidence to support a diagnosis of myocardial infarction. The authors offered the explanation that the Q waves in the precordial leads from the left side were due to fusion of potentials derived from the surfaces of the right and left ventricles in the transitional zone. This explanation can hold true only when no R deflection is present in the leads from the right side of the precordium.

We have made the diagnosis of anterior infarction in association with left bundle branch block for ten patients. Q waves were observed both in Lead I and in leads from positions on the extreme left side of the chest in six instances: in Lead I only in one; and in leads from the left side of the precordium only in one instance. Dependable evidence of myocardial infarction in the presence of left

bundle branch block—as in its absence[10]—is the combination of diagnostic changes of the QRS complex with significant features in the final ventricular complex. It was present in six out of ten patients for whom anterior infarction was diagnosed. It must be borne in mind, however, that certain features of left bundle branch block resemble closely those usually attributed to anterior infarction. These features of uncomplicated left bundle branch block are: 1) absent R waves or R deflections less than 1.0 mm. high in leads from the right side of the precordium; 2) marked elevation (up to 7.0 mm.) of the RS-T junction and unusually high (up to 19.0 mm.) T waves in chest leads from right precordial positions, where the S deflection predominates; and 3) inversion of the T wave in Lead I and in leads from the left side of the precordium. The inverted T waves have usually asymmetrical limbs and their RS-T junctions are slightly depressed. Occasionally when the transitional zone is broad and shows the features of the precordial pattern from the left rather than the right side of the heart, inversion of the T wave is observed as far to the right as Position C_4 or even C_3.

The following changes of the final ventricular complex are not encountered with "pure" left bundle branch block and are suggestive of complicating anterior infarction: 1) significant elevation of the RS-T junction in Lead I or in the chest leads, that is, elevation of the RS-T segment which is either preceded by a prominent R deflection or followed by a flat, diphasic (plus-minus), or inverted T wave; in precordial leads, which display a deep S wave, an elevation of the RS-T junction that measures more than 8 mm., or an elevated RS-T junction associated with a T wave, whose amplitude is less than twice the distance of the elevated RS-T junction from the level of reference; 2) significant (reciprocal) depression of the RS-T junction in Lead III, that is, a depression measuring more than one-sixth of the amplitude of the predominant QRS deflection in Lead III; 3) diphasic (plus-minus) or inverted T waves in those chest leads displaying a prominent S (QS) deflection; and 4) inverted T waves with symmetrical limbs and with RS-T junctions not depressed in Lead I and/or in leads from the left side of the precordium.

In the group of ten patients with anterior wall infarction complicating left bundle branch block, the most frequently encountered significant change of the final ventricular complex was an inverted T wave with symmetrical limbs and either isoelectric or elevated RS-T junction. This sign was observed in eight instances; in three it was present in Lead I and in precordial leads from the left side simultaneously; in four it was observed in Lead I only; and in one, only in the leads from the left side of the precordium. Next in frequency ranged significant elevation of the RS-T junction in the chest leads. It was present in seven. In three instances of infarction with left bundle branch block, prominent S waves in the chest leads were associated with plus-minus T waves. Significant depression of the RS-T junction in Lead III occurred only once (Case 5, Fig. 7) as a reciprocal change in the early stage of anterior infarction.

Posterior wall infarction.—In the presence of left bundle branch block, posterior infarction manifests itself more often by significant features in the final ventricular complex than by changes of the QRS complex. The diagnosis of posterior infarction on the basis of significant changes of the QRS complex encounters great difficulties even in those rare instances where the potential of the

left ventricular cavity may be negative at the beginning of systole because of extensive involvement of the interventricular septum. One reason is that even in uncomplicated left bundle branch block Q waves or QS deflections are commonly observed in Lead III. Lead III equals $V_F - V_L$. The unipolar lead from the left leg, when the heart is in the horizontal position (as it usually is in adults), resembles the leads from the right side of the precordium which often lack an R deflection. On the other hand, the unipolar lead from the left arm usually shows a shape similar to that of leads from the left side of the chest, that is, a prominent R deflection. The latter tends to produce a downward-directed initial stroke of the QRS complex in the combination $V_F - V_L$. Conditions are different in Lead II. Even when posterior infarction has caused a deep Q wave in the unipolar lead from the left leg, this need not necessarily produce a Q wave in Lead II, because in left bundle branch block the potential of the right arm is, as a rule, negative throughout the QRS complex and tends to cause an upward initial stroke in the ventricular complex in Lead II; for Lead II equals $V_F - V_R$.

Sodeman and associates[16] observed a QS deflection in Lead III in one-third of a group of unselected patients with left bundle branch block. In our series of patients with uncomplicated left bundle branch block, a QS deflection was present in Lead III in 25 per cent, and a small Q_3 deflection was observed in 10 per cent. Thus the finding of QS deflections or Q waves in Lead III has no significance for the diagnosis of posterior infarction unless it is associated with Q waves in Lead II. We have never observed a Q wave in Lead II when left bundle branch block was uncomplicated.

In the material of our study, posterior infarction was diagnosed in six patients. All of them but one (Case 9, Fig. 11) presented, in Lead III, QS deflections or Q waves. The latter showed in three tracings qualities that were not observed with uncomplicated left bundle branch block, such as marked slurring or notching, a duration of more than 0.03 second, and an amplitude as great as or greater than one-fourth the size of the succeeding R deflection. On the basis of the small material that was available for our study, it cannot be said whether or not these qualities of Q_3 as isolated features, are significant for the diagnosis of posterior infarction.

A Q wave in Lead II was absent in four out of six tracings obtained in posterior infarction. Case 6 (Fig. 8) is especially significant because post-mortem examination revealed extensive posterior wall infarction that involved the interventricular septum. Yet Q waves were absent in Lead II when left bundle branch block was present, and they appeared one day later, after the left bundle branch block had disappeared. Only a broad, slurred Q_3 was constantly observed in that patient, both in the presence and absence of left bundle branch block. Case 7 (Fig. 9) presented a QS deflection in Lead III and a W-shaped QRS complex in Lead II; the latter was in some beats preceded by a tiny upstroke (Q-wave equivalent). Post-mortem examination revealed recent infarction of the posterior portion of the interventricular septum and of the entire posterior wall of the right ventricle. It may be that in this case involvement of the right ventricle was responsible for the appearance of a W-shaped QRS complex in Lead II, which

we consider as significant since we have not observed a similar shape of the QRS complex in Lead II in any of the other tracings in left bundle branch block.

Besides the finding of a QS deflection or Q wave in Lead III, uncomplicated left bundle branch block has in common with posterior infarction some features of the final ventricular complex: 1) elevation of the RS-T junction in Leads II and III; 2) depression of the RS-T junction in Lead I and in leads from the left side of the precordium; and 3) inversion of the T wave in Leads II and III.

The following changes of the final ventricular complex in the presence of left bundle branch block may be considered as suggestive of posterior infarction: 1) elevation of the RS-T junction in Lead III (and II) when it follows an R wave or when it measures more than one-sixth of the amplitude of the preceding S deflection; 2) depression of the RS-T junction in Lead I and/or in the precordial leads from positions over the left side, when it measures more than one-seventh of the amplitude of the preceding R deflection; 3) depression of the RS-T junction in chest leads displaying a prominent S (QS) deflection; 4) "coronary T waves" in Leads II and III; and 5) inverted T waves in both Leads II and III when the amplitude of T_3 is more than 3.0 millimeters.

Significant elevation of the RS-T junction was observed in Leads II and III in two instances of posterior infarction (Case 6, Fig. 8 and Case 8, Fig. 10); in Lead III only, in two instances (Case 9, Fig. 11 and Case 10, Fig. 12). Significant depression of the RS-T junction in chest leads presenting a deep S or QS deflection was a leading sign of acute posterior infarction in three patients (Case 6, Fig. 8; Case 8, Fig. 10; and Case 9, Fig. 11). "Coronary T waves" were observed in Leads II and III in one patient (Case 10, Fig. 12). In one instance (Case 6, Fig. 8) the amplitude of the inverted T_3 was slightly more than 3.0 millimeters.

In clinical practice, patients with left bundle branch block without evidence of complicating myocardial infarction and especially without symptoms of anginal distress are scarce. It is obvious that it is difficult to evaluate for statistical purposes such small material as is presented in this report. Further clinical and pathologic investigation on a large scale will be required in order to establish conclusively the signs of myocardial infarction in combination with left bundle branch block as distinguished from the features of uncomplicated left bundle branch block.

SUMMARY

Forty-three patients with left bundle branch block were studied, twenty-eight of whom appeared to have "uncomplicated" left bundle branch block, that is, they presented neither a history of myocardial infarction nor symptoms of anginal character associated with effort or rest. In fifteen patients evidence of myocardial infarction was obtained, either by necropsy or by electrocardiographic signs observed in tracings prior to the development of left bundle branch block or after its disappearance, or by a characteristic history suggestive of myocardial infarction in conjunction with confirmatory clinical and laboratory evidence. In nine patients anterior infarction was diagnosed, in five, posterior infarction, and in one, the signs of anterior and posterior infarction were combined.

By comparing the tracings of "uncomplicated" left bundle branch block with records presenting evidence of complicating myocardial infarction, certain features

were discerned which appeared to be suggestive of myocardial infarction in association with left bundle branch block.

Uncomplicated left bundle branch block has some features in common with anterior wall infarction: 1) Q waves in Lead I and/or in leads from the left side of the precordium (very rare); 2) absent R waves (QS deflections) or R waves less than 1 mm. high in leads from the right side of the precordium; 3) marked elevation (up to 7 mm.) of the RS-T junction and high T waves (up to 19 mm.) in leads from the right side of the precordium which display deep S waves or QS deflections; and 4) inverted T waves in Lead I and/or in leads from the left side of the precordium which, in the presence of uncomplicated left bundle branch block, usually display asymmetrical limbs and slightly depressed RS-T junctions.

The following features were considered as suggestive of anterior wall infarction in the presence of left bundle branch block.

1) Q waves in Lead I and/or in precordial leads from left-side positions, especially when R deflections are present in the precordial leads from the right side.

2) Elevation of the RS-T junction in Lead I or in the chest leads, when it is either preceded by a prominent R deflection or followed by flat, diphasic (plus-minus) or inverted T waves; in precordial leads displaying deep S or QS waves, when the elevation of the RS-T junction measures more than 8 mm. or when it is followed by a T wave whose amplitude is less than twice the distance of the elevated RS-T junction from the level of reference (in the absence of digitalis eflect).

3) Reciprocal depression of the RS-T junction in Lead III, when it measures more than one-sixth of the amplitude of the predominant QRS deflection in Lead III.

4) Diphasic (plus-minus) or inverted T waves in those chest leads displaying a deep S or QS deflection.

5) Inverted T waves with symmetrical limbs and RS-T junctions not depressed in Lead I and/or in chest leads from left-side positions.

Posterior wall infarction has some features in common with left bundle branch block: 1) Q waves or QS deflections in Lead III; 2) elevation of the RS-T junction in Leads II and III; 3) depression of the RS-T junction in Lead I and in leads from the left side of the precordium; and 4) inversion of the T wave in Leads II and III.

The following features were considered as suggestive of posterior infarction in the presence of left bundle branch block.

1) Q waves or QS deflections in Lead III in conjunction with Q waves or W-shaped QRS complexes (or Q wave equivalents) in Lead II.

2) Elevation of the RS-T junction in Lead III (and II), when it follows an R deflection or when it measures more than one-sixth of the amplitude of the S deflection in the same lead.

3) Depression of the RS-T junction in Lead I and/or in chest leads from the left positions, when it measures more than one-seventh of the amplitude of the preceding R deflection.

4) Depression of the RS-T junction in chest leads displaying a prominent S or QS deflection.

5) Coronary T waves in Leads II and III.

6) Inversion of the T wave in Leads II and III, when the inverted phase in Lead III measures more than 3 millimeters.

Post-mortem examination was obtained for two patients with anterior infarction and two with posterior infarction. The tracings of these patients showed significant Q waves or Q-wave equivalents. The interventricular septum was involved in all. These findings support the assumption of Wilson that infarction of the interventricular septum may be an important factor in the development of significant Q waves when left bundle branch block is present.*

ADDENDUM

Since this paper was submitted for publication in July, 1948, diagnostic features of myocardial infarction in the presence of bundle branch block were pointed out by W. Somerville and P. Wood (Brit. Heart J. **11**:305, 1949).

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*Since this paper was finished two more patients were observed in whom the electrocardiogram showed left bundle branch block and Q waves significant of myocardial infarction. In one patient anterior wall infarction was diagnosed, in the other anterior and posterior infarctions. The diagnosis was confirmed by post-mortem examination which in both instances revealed extensive involvement of the interventricular septum.

DIFFICULTIES IN THE ELECTROCARDIOGRAPHIC DIAGNOSIS OF MYOCARDIAL INFARCTION

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THE clinical picture associated with coronary thrombosis was first clearly defined by Herrick in 1912.[1] Following this the typical and atypical[2] clinical features resulting from coronary occlusion were described in detail. During the past two decades emphasis has been focused on the electrocardiographic patterns produced in this condition. The earliest electrocardiographic classifications[3,4] of myocardial infarction included only anterior and posterior localizations. Since then, the electrocardiographic picture of myocardial infarction involving the anteroseptal,[5] anterolateral, posterolateral, posteroinferior, high lateral,[6] and septal involvement extending from the anterior to the posterior aspects of the heart[7] have been clearly defined and correlated with post-mortem findings. The electrocardiographic patterns resulting from auricular infarction,[8] and from the presence of infarction limited to the right ventricle,[9] have also been described.

The purpose of the present article is to describe those conditions in which electrocardiographic diagnosis of myocardial infarction might be rendered difficult. Most of the material for this report was secured by making comparisons between the electrocardiographic interpretations and the pathologic change in the hearts of patients who were found to have myocardial infarcts at necropsies performed at the Charity Hospital of Louisiana in New Orleans during the two years prior to this report. There were 519 patients admitted during this period for whom the diagnosis at the time of discharge or death was myocardial infarction. One hundred sixty-four of these patients died, and post-mortem examination was performed on sixty-one. There were thirteen instances of marked discrepancy between the electrocardiographic interpretation and the autopsy findings.

Routine electrocardiograms consist of at least the three standard leads and the precordial leads V_1 through V_6. In certain patients the potential was determined at the ensiform cartilage, at the anterior and lateral aspects of the left third and fourth intercostal spaces, across the posterior chest wall, at various other points on the chest wall, and in the esophagus. The electrocardiograms were re-examined whenever the post-mortem findings did not confirm our electrocardiographic interpretation, in order to see if any satisfactory explanation for the discrepancy could be found.

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The errors in electrocardiographic diagnosis of myocardial infarction might be placed in three groups: (1) infarction not recognized; (2) infarction not localized correctly; and (3) infarction misdiagnosed.

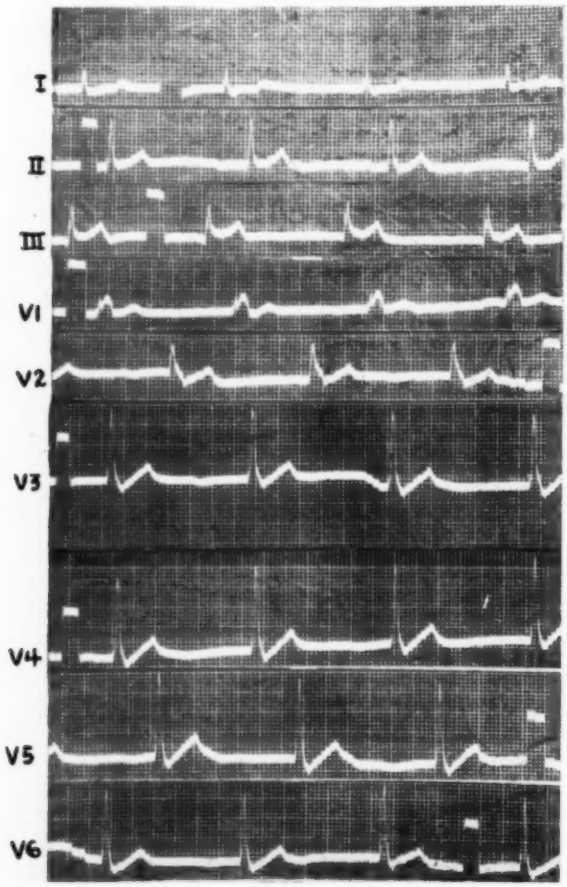

Fig. 1.—Patient J. B. ECG shows a complete heart block with an idioventricular rhythm. Necropsy revealed a 4- by 5-cm. area of infarction limited to the septum, which on microscopic sections showed diffuse myocardial degeneration.

INFARCTION MISSED OR NOT LOCALIZED

"Silent" or Relatively Silent Regions

Septum.—The electrocardiogram on Patient J. B. (Fig. 1) shows a complete heart block with idioventricular rhythm. At post-mortem examination infarction limited to the septum was found. There are certain regions of the myocardium where absence of activation due to dead muscle may not cause readily recognizable changes in the limb leads or six standard precordial leads. One of these areas is the septum. A lesion, if limited to the septum, will not necessarily

produce electrocardiographic changes which can be interpreted as evidence of myocardial infarction. Although bundle branch block (Fig. 7), complete heart block, or prolongation of the P-R interval may result, these findings alone cannot be considered as electrocardiographic confirmation of a diagnosis of coronary occlusion.

From theoretical considerations one might expect to observe disappearance of the normal small Q_1 in counterclockwise rotated* hearts (or of Q_3 in clockwise rotated hearts) in which the septum is infarcted with resulting absence of the initial electromotive forces due to activation of the septum. These initial forces are normally so oriented that positivity is directed toward the right side of the septum, this being attributable to either earlier activation or a larger area of simultaneous activation on the left side of the septum. The absence of the initial R wave in leads from the right ventricle obtained by cardiac catheterization might suggest septal infarction. Septal infarctions which extend to the anterior or to the posterior walls usually produce characteristic electrocardiographic patterns. Recently, the electrocardiographic picture of septal infarction extending to both the anterior and posterior aspects of the heart has been described.[6] Electrocardiographic changes indicating simultaneous involvement of the anterior and posterior walls adjacent to the septum suggest this diagnosis.

High Posterior.—The electrocardiogram on Patient A. S. (Fig. 2) shows only RS-T segment elevation in Leads I and V_6, and depression of the segment in V_2, V_3 and V_4; post-mortem examination, however, revealed a hemopericardium due to leakage from a 5-cm. area of infarction on the posterior aspect of the left ventricle, extending inferiorly from the A-V junction. Infarction involving the superior portion of the posterior wall of the left ventricle adjacent to the A-V junction may not cause changes in the electrocardiogram, since absence of normal electrical activity in this region may not result in QRS changes characteristic of infarction. This is especially true in clockwise rotated, "apex-back," vertical hearts, in which the resultant electrical components derived from this area are normally directed largely peripendicularly to the frontal plane. Esophageal electrocardiograms might be helpful in this type of patient.

High Lateral.—The electrocardiogram taken on Patient J. R. (Fig. 3) shows characteristic QRS changes in leads taken above the usual V_1 through V_6 positions. Myocardial infarction involving the superior portion of the lateral wall of the left ventricle may be missed unless precordial leads are taken in areas above the usual V_4 through V_6 positions. This area of infarction has been designated high lateral infarction.[6]

Right Ventricle.—The electrocardiograms on patient L. F. (Fig. 4) show a QS wave in V_1, V_2, and V_3, and possible incomplete left bundle branch block. On post-mortem examination massive infarction of the right ventricle with septal

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*In this paper the terminology employed by Gardberg and Ashman[10] for rotation of the heart on its three axes will be utilized. Rotation on the anteroposterior axis will produce vertical or horizontal positions. Rotations on the longitudinal anatomic axis as viewed from the apex will produce clockwise or counterclockwise rotated heart positions. Rotation about the transverse axis will produce an apex forward or apex back position.

involvement was found. Infarctions involving the right ventricle may be suggested by changes in V_1 and leads taken superior to the V_2 and V_3 positions.

Auricular.—Changes in the P wave and P-R segment have been described

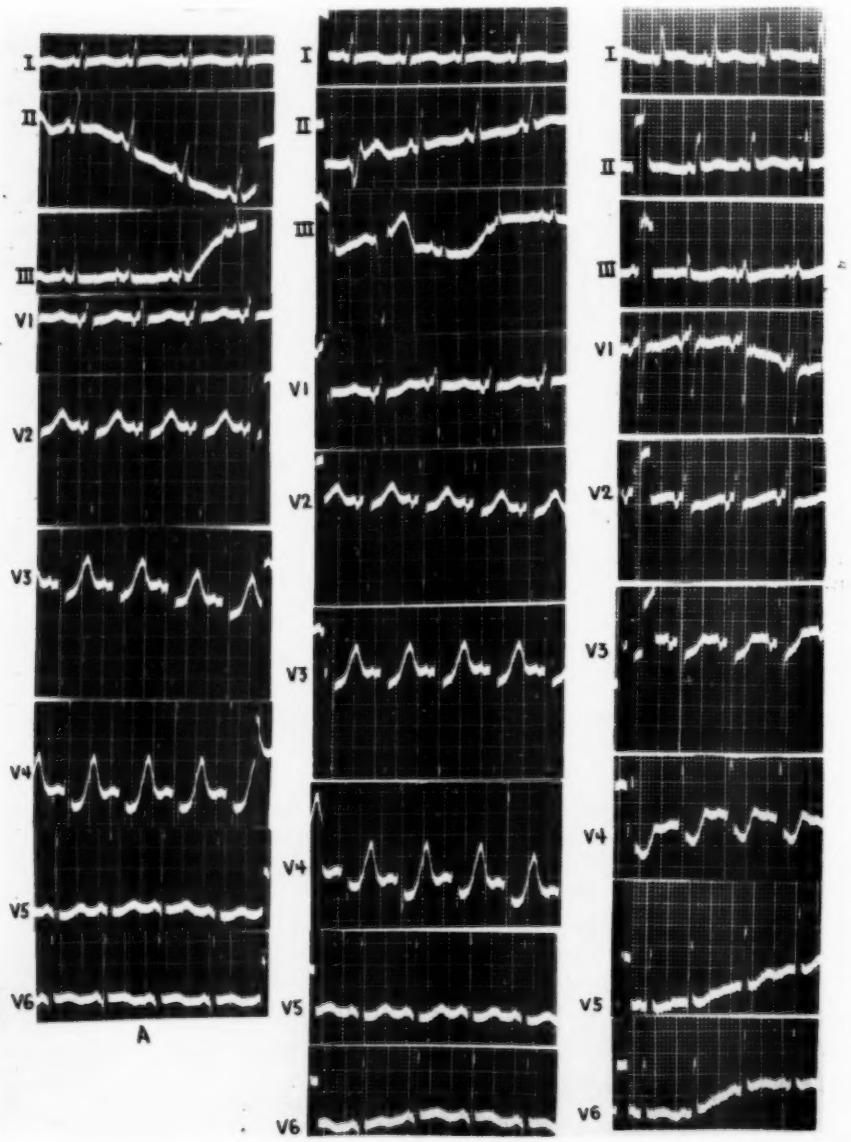

Fig. 2.—Patient A. S. *A*, *B*, and *C*, three tracings taken on successive days, the last just prior to death. The only abnormal findings were elevation of the RS-T segment of Lead I, elevation in V_6, and depression in V_2, V_3, and V_4. Necropsy revealed a 5-cm. area of transmural infarction on the posterior aspect of the left ventricle extending from the A-V junction inferiorly. In the center of the infarcted area there was an area of ulceration of the epicardium from which blood had oozed that was the source of a hemopericardium.

in auricular infarction. In none of our patients with auricular involvement were these changes demonstrated, although an ectopic pacemaker appeared in Patient E. W. (Fig. 6) who had an area of infarction involving the right auricle.

Small Anterior Infarctions

The electrocardiogram on Patient A. W. (Fig. 5) shows relatively low R waves in V_2 and V_3. At necropsy there was found a 3- by 4-cm. myocardial

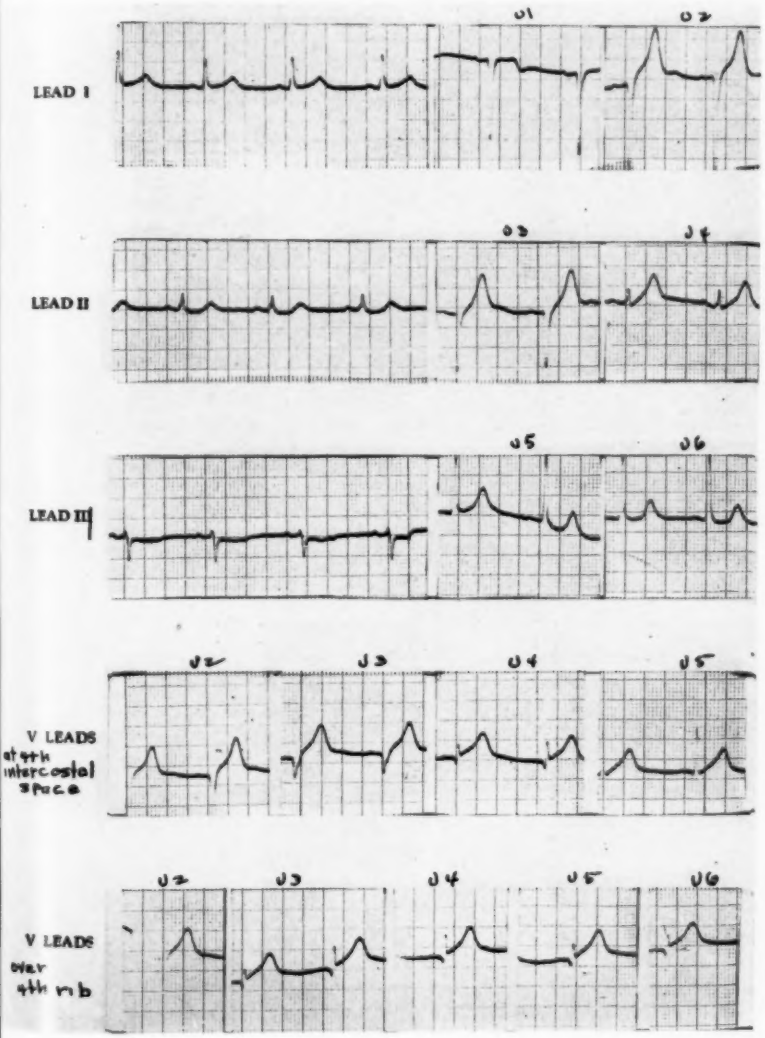

Fig. 3.

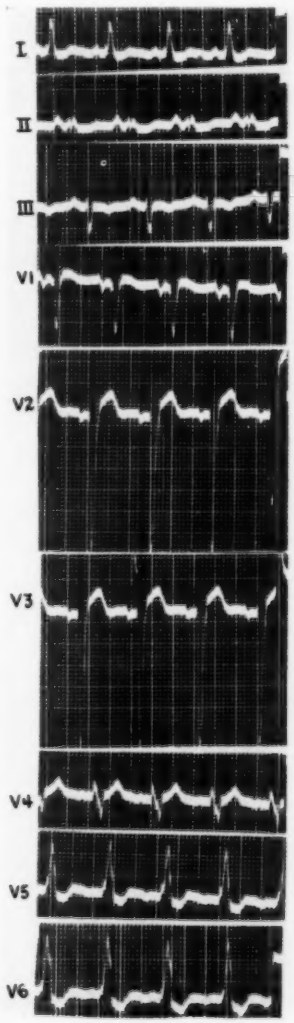

Fig. 4.

Fig. 3.—Patient J. R. The routine ECG showed a QS complex in V_1, V_2, and V_3 with high T waves in V_4 and V_5. The tracings taken at the level of the fourth intercostal space showed QRS changes more characteristic of myocardial infarction.

Fig. 4.—Patient L. F. A QS complex is present in V_1, V_2, and V_3 with possible incomplete left bundle branch block. Necropsy revealed an area of massive infarction of the right ventricle with septal involvement.

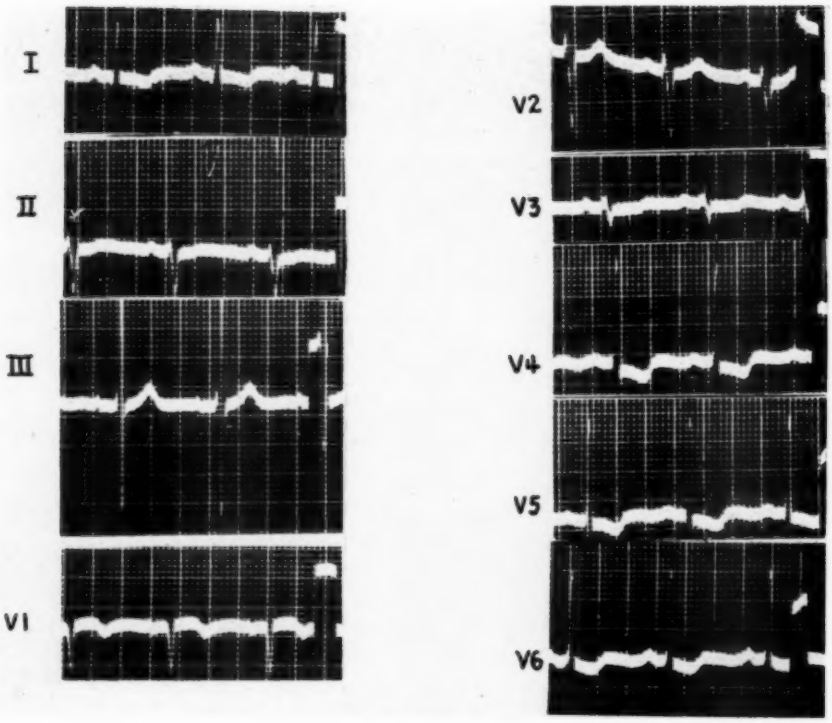

Fig. 5.—Patient A. W. ECG is compatible with left ventricular hypertrophy. This patient was receiving digitalis. R waves in V_2 and V_3 are of relatively low amplitude. Necropsy revealed a 3- by 4-cm. area of recent infarction anteriorly just to the left of the interventricular groove near the apex.

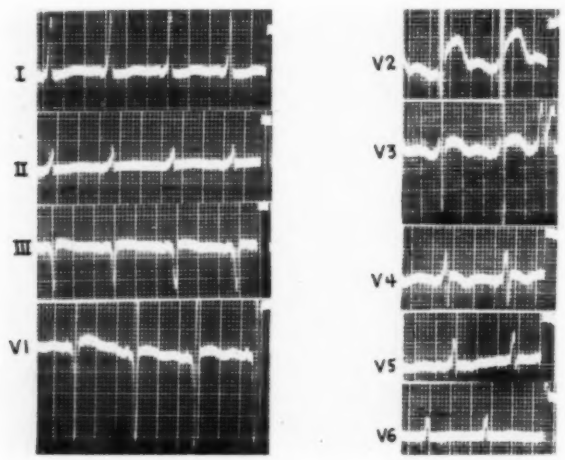

Fig. 6.—Patient E. W. ECG is compatible with left ventricular hypertrophy. There is an ectopic pacemaker; a previous tracing showed a P-R interval of 0.16 seconds with the same QRS configuration. There is a relatively small R wave in V_2 and V_3 with a deep S wave and elevated RS-T segment. This patient was receiving digitalis. Necropsy revealed a 3-cm. area of infarction with softening of the anterior surface of the left ventricle near the apex. There was a friable mural thrombus adherent to the endocardium in this area. There was also an area of infarction involving the right auricle. The lumen of the anterior descending branch of the left coronary artery was occluded.

infarction anteriorly just to the left of the interventricular groove. The electrocardiogram on Patient E. W. (Fig. 6) shows relatively low R waves in V_2 and V_3. At post-mortem examination there was a 3-cm. area of infarction with softening of the anterior surface of the left ventricle. In certain patients with small areas

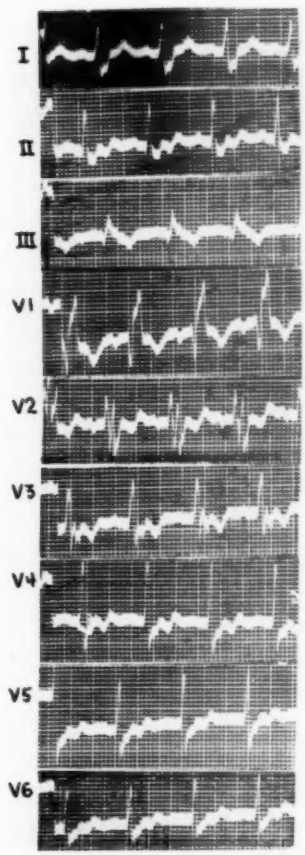

Fig. 7.—Patient O. J. Right bundle branch block is present. In all sections of the left ventricle and interventricular septum, necropsy revealed numerous myocardial infarctions, averaging approximately 1.0 by 2.0 cm. in size. Some of these extended inward from the epicardium and outward from the endocardium for varying distances. Some of the areas were completely intramural; however, none were transmural.

of anterior myocardial infarction the electrocardiogram may not be characteristic of infarction. The failure of the R wave to increase in amplitude in the usual fashion as the electrode is moved from the right to the left precordium, or the presence of a QS wave in V_1 and V_2, may be attributed to left ventricular hypertrophy or to an "apex-back" position of the heart.[10] The presence of an initial R wave in Lead V_{3R} and V_E when a QS complex is present in V_1 and V_2 may help to indicate the presence of an anterior infarct.[11]

Small Infarctions

The electrocardiogram of Patient O. J. (Fig. 7) shows right bundle branch block and T-wave changes suggestive of myocardial ischemia. Necropsy re-

vealed numerous myocardial infarctions, averaging about 1.0 by 0.2 cm. in size, in all sections of the left ventricle and interventricular septum. Scattered small infarcts in the left ventricle should not produce characteristic changes suggesting myocardial infarction, since the absence of electrical effects in these areas will not cause sufficient alteration in the pathway of the wave of accession to result in an electrocardiographic pattern suggesting myocardial infarction.

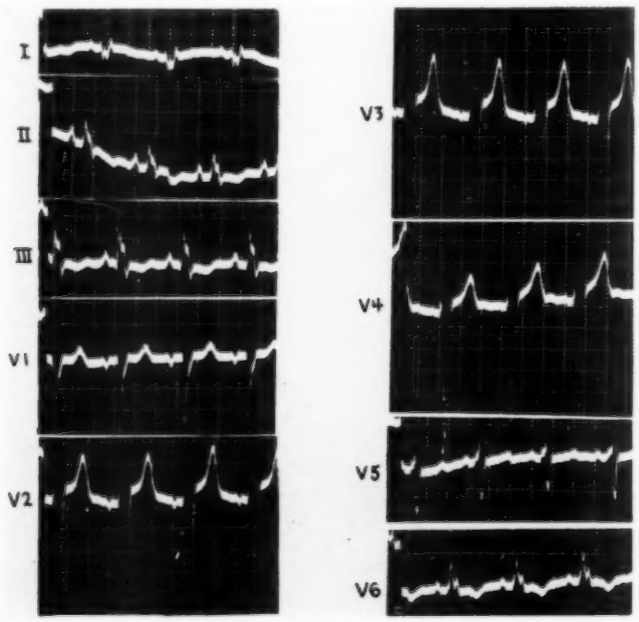

Fig. 8.—Patient A. V. B. The wide QRS complexes suggest block either in the left bundle branch or in the left ventricular muscle. The low amplitude of the R wave in V_2 through V_5 and the QRS configuration in Lead I suggest the possibility of an anterolateral lesion. Necropsy revealed a 5-cm. area of old infarction on the posterolateral wall of the left ventricle extending transmurally. There was a recent 2-cm. area of infarction involving the apical region and extending transmurally.

Multiple Infarctions

The post-mortem examination of Patient A. V. B. (Fig. 8) revealed an area of old infarction involving the posterior wall of the left ventricle. There was also an area of recent infarction involving the apical region. The electrocardiographic evidence of posterior infarction was obscured. There are patients who have multiple areas of infarction in which the effects of one area predominate and make the diagnosis of multiple areas of infarction impossible. In rare instances there are two areas of myocardial infarction of similar size involving diametrically opposed areas of the left ventricle, so that the electrical changes in one wall are to some extent counterbalanced by change in the opposite wall. Serial studies of patients with multiple episodes of myocardial infarction will usually enable one to localize the lesion accurately, despite the fact that the final electrocardiogram may show QRS changes of the predominant area of infarction only.

Intramural Infarctions

The tracing of Patient V. M. (Fig. 9) shows no abnormalities to suggest myocardial infarction. At post-mortem examination a large intramural infarction was found involving most of the posterior wall of the left ventricle. It is interesting to note that the QRS magnitude found in leads taken over the

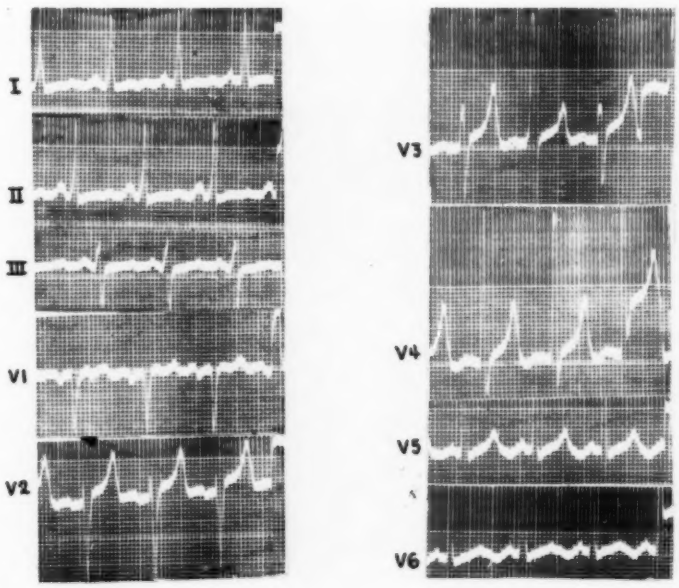

Fig. 9.—Patient V. M. ECG is compatible with left ventricular hypertrophy. T waves in V_2, V_3, and V_4 are high. Necropsy revealed an ovoid area of infarction, the superior edge of which was 1.0 cm. below the intersection of the interventricular septum and the base of the left ventricle, and which extended posteriorly for a distance of 9 centimeters. The area of infarction was 6.0 cm. in width and ended 2.0 cm. above the apex on the lateral surface of the left ventricle. It was completely intramural and did not reach the epicardial surface.

posterior chest wall in this patient was well below the average range of QRS magnitudes found in a large series of normal patients.[12] A region of infarction which is completely intramural will usually not cause characteristic changes associated with myocardial infarction. The wave of accession will be altered, but the initial forces of activation in the subendocardial areas may cause an upright deflection in the leads which face the area of infarction, so that the prominent Q wave, suggesting dead muscle tissue, is absent. The effects of "injury" in a completely intramural infarction may also not produce characteristic RS-T segment displacements. Post-mortem examination of Patient M. W. (Fig. 10) showed an area of infarction on the lateral aspect of the heart involving the outer third of the myocardium. The electrocardiogram shows a prominent, wide S wave in Leads V_4 and V_5. Post-mortem examination on Patient J. H. (Fig. 11) showed a 4.5-cm. area of old infarction on the posterolateral aspect of the left ventricle extending from the epicardium inward and involving the outer one-half

of the myocardium. The electrocardiogram shows a prominent S wave in Leads II, III, and V_4, V_5, and V_6. If an area of infarction extends from the epicardium inward and involves only about one-half of the myocardium, the QRS changes

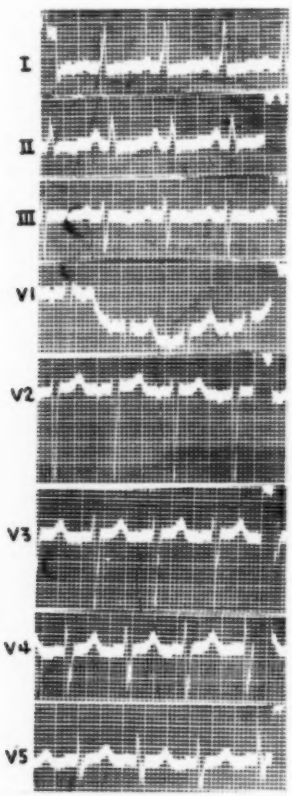

Fig. 10.—Patient M. W. R_1 is slurred and a notched S wave is present in V_4 and V_5. This tracing was interpreted as being suggestive of left ventricular hypertrophy. Necropsy revealed an oval, 3-cm. area of infarction on the lateral aspect of the heart involving the outer third of the myocardium.

may not suggest infarction. Since the initial spread of excitation from the endocardium outward is not affected in this type of lesion, a Q wave will not appear and only a reduction in the amplitude of the R wave or the appearance of an S wave in the leads which face the infarcted area may occur.

Obscuration of Typical Changes

Bundle Branch Block.—In the presence of bundle branch block the characteristic QRS changes produced by myocardial infarction are modified. Bundle branch block may in itself be due to the presence of septal infarction (Fig. 7). In left bundle branch block the electrocardiographic changes indicating myocardial infarction are rarely diagnostic. If left bundle branch block is present, initial activation of the septum occurs on its right side, and the left arm and left lateral precordium face the positive side of the wave of accession. This results

in an absence of a Q wave in Lead I and in the left lateral precordial leads in most cases. The appearance of a Q wave in these leads in left bundle branch block suggests the possibility of septal infarction;[13] however, this may also occur as a result of clockwise rotation of the heart on its longitudinal axis as viewed from the apex.[14] Although, in the presence of left bundle branch block, a diagnosis of septal infarction has been suggested in two of our patients on the basis

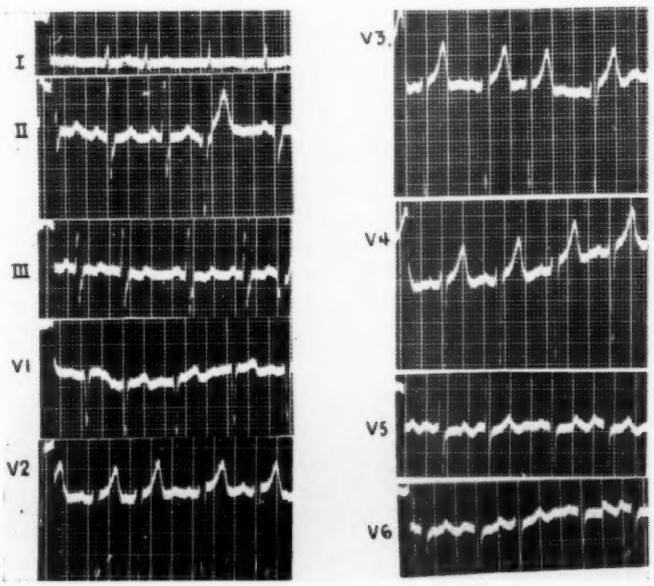

Fig. 11.—Patient J. H. ECG showed a prominent, slurred S wave in Leads II and III and in V_4, V_5, and V_6. Necropsy revealed an area of old infarction 4.5 cm. in diameter on the posterior lateral aspect of the left ventricle extending from the epicardium inward and involving only the outer half of the myocardium.

of prominent Q wave in Lead I and in the left precordial leads, neither of the patients with this electrocardiographic picture has had post-mortem examination. In some of our patients whose electrocardiograms show left bundle branch block the appearance of segment shifts due to the effects of injury, and variability in the QRS configuration in serial electrocardiograms over a period of weeks, suggest the presence of myocardial infarction. Since none of these patients had post-mortem examinations we were not able to confirm our interpretation. Right bundle branch block usually does not obscure the changes produced by infarction of the left ventricle.

Ventricular Tachycardia.—There are two patients with myocardial infarction in our series in whom initial electrocardiograms show ventricular tachycardia. One of these (W. M.) had no history to suggest infarction. The post-mortem examination on Patient G. P. (Fig. 12) showed an area of recent infarction involving the apex of the septum and the surrounding circumapical area of ventricular muscle. The post-mortem examination of Patient W. M. (Fig. 13)

showed an area of recent massive infarction involving the posterior, lateral, and circumapical areas of the left ventricle. Paroxysmal ventricular tachycardia may render the electrocardiographic diagnosis of myocardial infarction difficult.

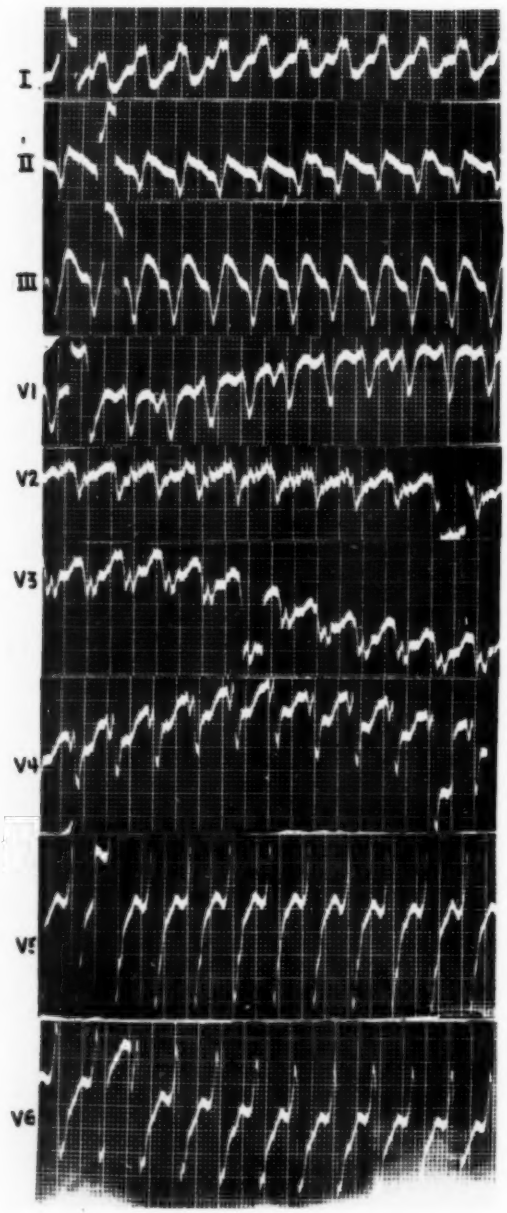

Fig. 12.—Patient G. P.: ECG reveals ventricular tachycardia with an independent auricular rhythm. Necropsy showed an area of necrotic degeneration of the myocardium at the apex of the septum and the surrounding circumapical area of the ventricle. The infarct was transmural and measured 3.0 cm. in diameter on its left ventricular aspect and 1.5 cm. in diameter on the right ventricular aspect. There was a thrombosis of the right coronary and circumflex branch of the left coronary with marked atherosclerotic changes.

Although the appearance of ventricular tachycardia itself may suggest a diagnosis of myocardial infarction, the presence of this arrhythmia may preclude electrocardiographic confirmation of the diagnosis.

Other Conditions.—In complete heart block with an idioventricular rhythm, or in any mechanism disturbance in which initial activation occurs in the ventricles, the QRS changes due to infarction may be masked.

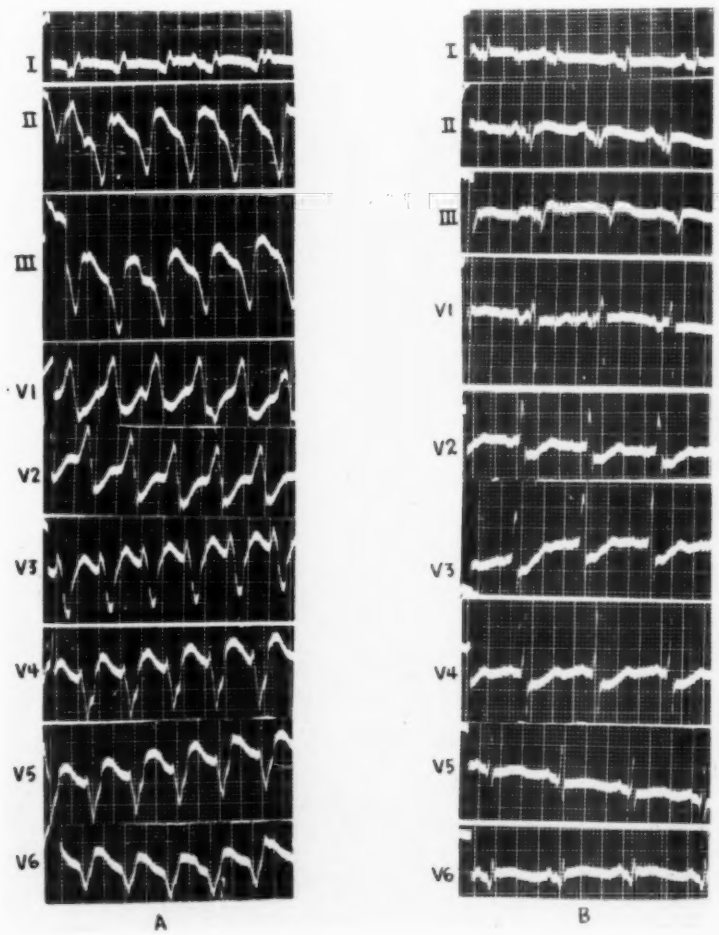

Fig. 13.—Patient W. M. Tracing *A* shows a ventricular tachycardia. *B*, taken after quinidine had been administered, shows QRS changes compatible with posterolateral myocardial infarction. This diagnosis was also suggested by changes in the first ECG. Necropsy revealed an ovoid 5-cm. area of massive transmural infarction involving the apical region and extending to the posterolateral surface of the left ventricle. It extended to within 1 cm. of the septum anteriorly and posteriorly extended superiorly to approximately 3 cm. below the A-V junction. There was a sclerotic plaque occluding the left anterior descending coronary artery.

Impending Infarction

We have observed one patient (E. W.) (Fig. 14) whose electrocardiogram shows characteristic QRS changes and RS-T segment shifts indicating anterolateral myocardial infarction, in whom necropsy, including detailed microscopic

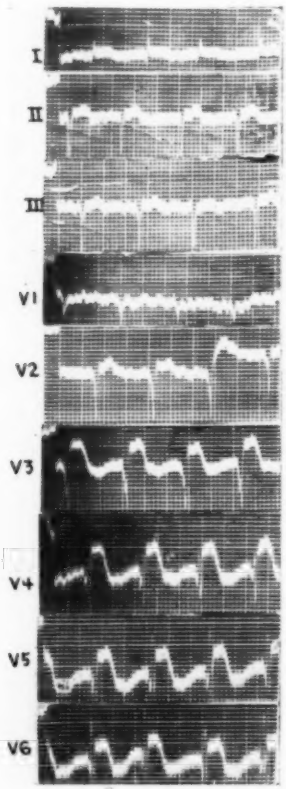

Fig. 14.—Patient E. W. The cardiogram shows QRS and RS-T changes which are diagnostic of anterolateral myocardial infarction. At necropsy marked stenosis of both coronary ostia was found; however, there were no myocardial changes to suggest infarction on gross examination or on microscopic examination of all sections taken. Special attention was directed toward the anterolateral wall of the left ventricle, and numerous sections were made.

sections, did not reveal any areas of myocardial infarction although there was stenosis of both coronary ostia. In rare instances the electrocardiographic picture usually associated with recent myocardial infarction may be seen when no area of myocardial infarction can be found at post-mortem examination. Although the electrocardiogram may show the pattern of recent myocardial infarction, actual death of the muscle may not have occurred before exitus. Hence, at post-mortem examination, tissue destruction may not be evident, although minor alterations in the muscle fibers may be detectable.[15] In these

cases the fibers in the involved region are severely injured, but not dead. The Q waves, of the type seen in infarction, may then be ascribed to slow invasion of the affected area by the wave of excitation together with a state of partial depolarization of the "injured" muscle. Blocking of the wave of excitation within the area may or may not occur.

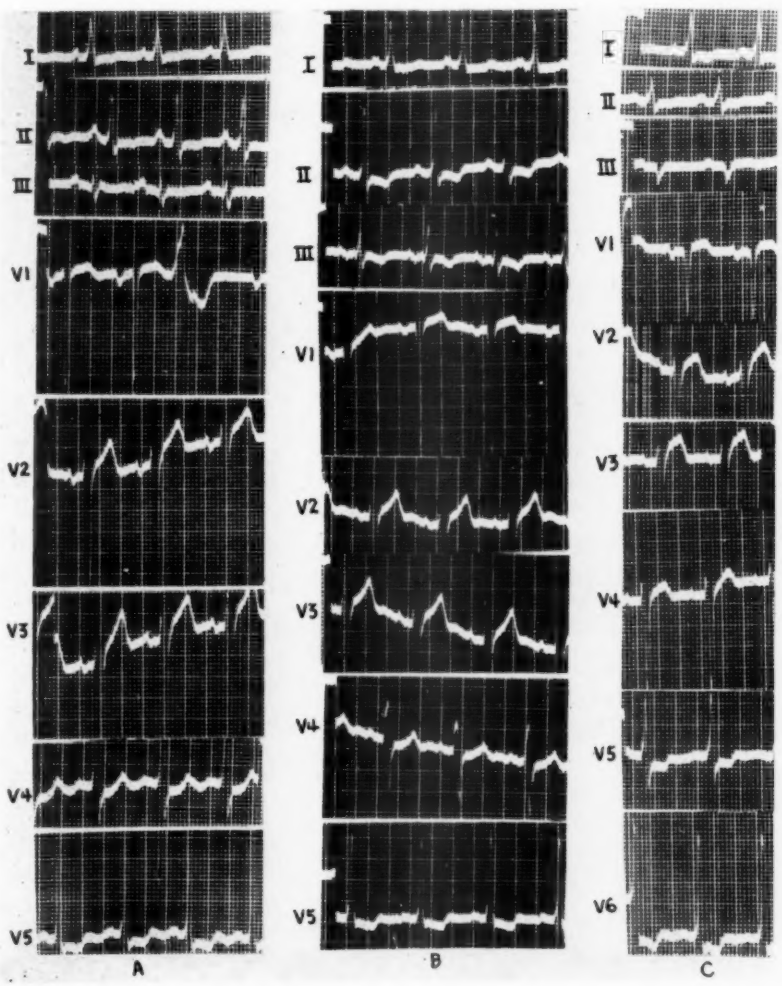

Fig. 15.—Patient B. H. The first tracings, *A* and *B*, were taken prior to the development of severe chest pain and were interpreted as being compatible with left ventricular hypertrophy. The patient was receiving digitalis. Following a clinical episode of chest pain, the third tracing (*C*) was taken and revealed the appearance of a QS deflection in Lead III with the disappearance of R_3. Necropsy revealed multiple areas of pulmonary infarction resulting from pulmonary emboli. There was no evidence of myocardial infarction on gross or microscopic examination of the heart, although a moderate degree of left ventricular hypertrophy was present.

Changes in Muscle Not Due to Coronary Atherosclerosis

Conditions other than atherosclerotic disease of the coronary arteries should be mentioned in a discussion of myocardial infarction. Electrocardiograms made during attacks of angina pectoris may closely simulate those recorded in

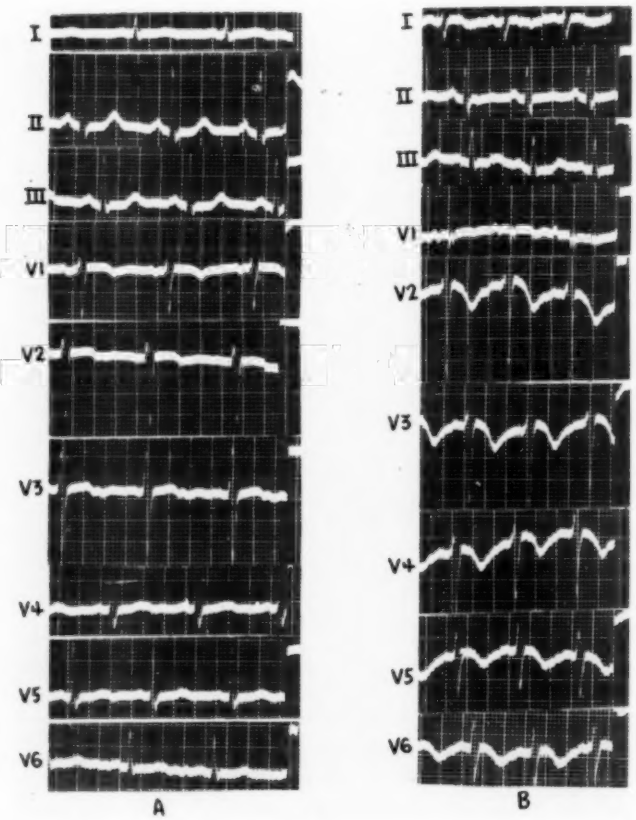

Fig. 16.—Patient G. K. The first ECG (*A*) was taken prior to a gastric resection and was interpreted as being within possible normal limits. The second ECG (*B*) was taken two days postoperatively when the patient developed sudden substernal pain. It revealed a marked right axis deviation with a small R_I and inverted T waves in Lead I and the precordial leads. There was a marked change in the QRS configuration in all leads except Lead III.

the early stages of myocardial infarction.[16] An electrocardiographic picture of myocardial infarction may result from occlusion of the coronary arteries due to various types of embolism (such as air, fat, and those composed of caseous matter[17]), or from disease of the wall of the coronary arteries (such as that due to extrinsic pressure, Buerger's disease, periarteritis nodosa, anaphylactic conditions, or rheumatic arteritis, syphilitic arteritis, or any other infectious process). Metastatic carcinoma, primary neoplasms of the heart, tuberculoma, gumma, trauma, and other conditions which cause a localized destruction of heart muscle might produce an electrocardiographic picture similar to that of infarction.

Pulmonary Embolism

The serial tracings on Patient B. H. (Fig. 15) show the appearance of a prominent Q_3. At post-mortem examination multiple pulmonary emboli were found but no evidence of myocardial infarction. Electrocardiograms taken on patients with pulmonary embolism occasionally resemble the pattern of pos-

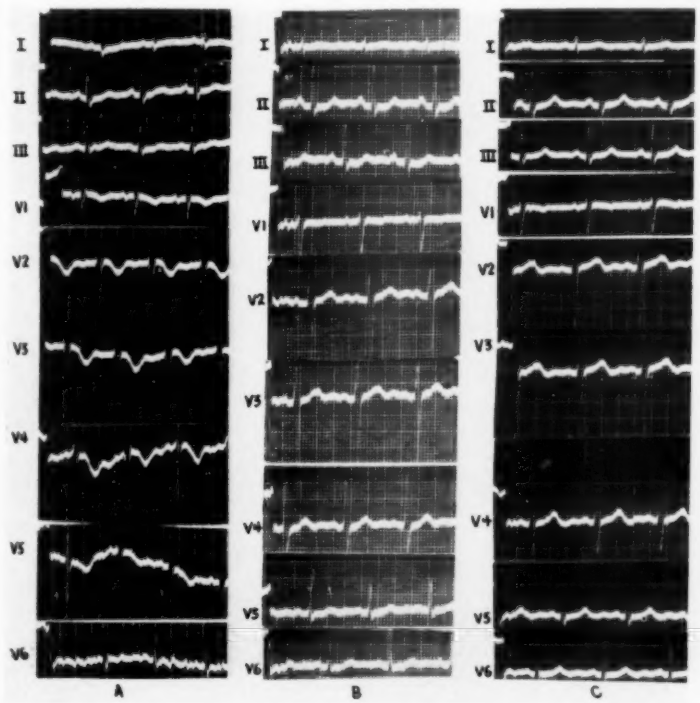

Fig. 17.—Patient G. K. (con't.). The first ECG (*A*) was taken four days after the pulmonary embolism. *B* was taken seven weeks later, and *C* was taken eight weeks subsequently. These tracings show a gradual return to the original pattern.

terior infarction. Inversion of the T waves in leads over the right ventricle and serial tracings will often help in the differentiation of these two conditions. Occasionally infarction in other areas of the myocardium may be simulated by pulmonary infarction. The serial electrocardiograms on Patient G. K. (Figs. 16 and 17) reveal a sudden development of a prominent S wave in Lead I together with a marked right axis deviation and prominent S waves over the precordium. Subsequent pictures show a return of the QRS configuration to its previous form. This patient had a pulmonary embolism following a gastric resection. The appearance of a marked right axis deviation with prominent S waves over the precordium can be explained on the basis of right ventricular dilatation with rotation of the heart clockwise as viewed from the apex, so that the right ventricle faces the anterior and lateral portions of the left side of the chest, and the left ventricle is displaced to the right and posteriorly. Serial electrocardiograms on

Patient F. I. (Fig. 18) show similar marked QRS changes following pulmonary embolism. The appearance of a large S wave in Leads I, V_5, and V_6, and a relatively high R wave in Leads III and V_1 resulted from right ventricular dilatation with clockwise rotation.

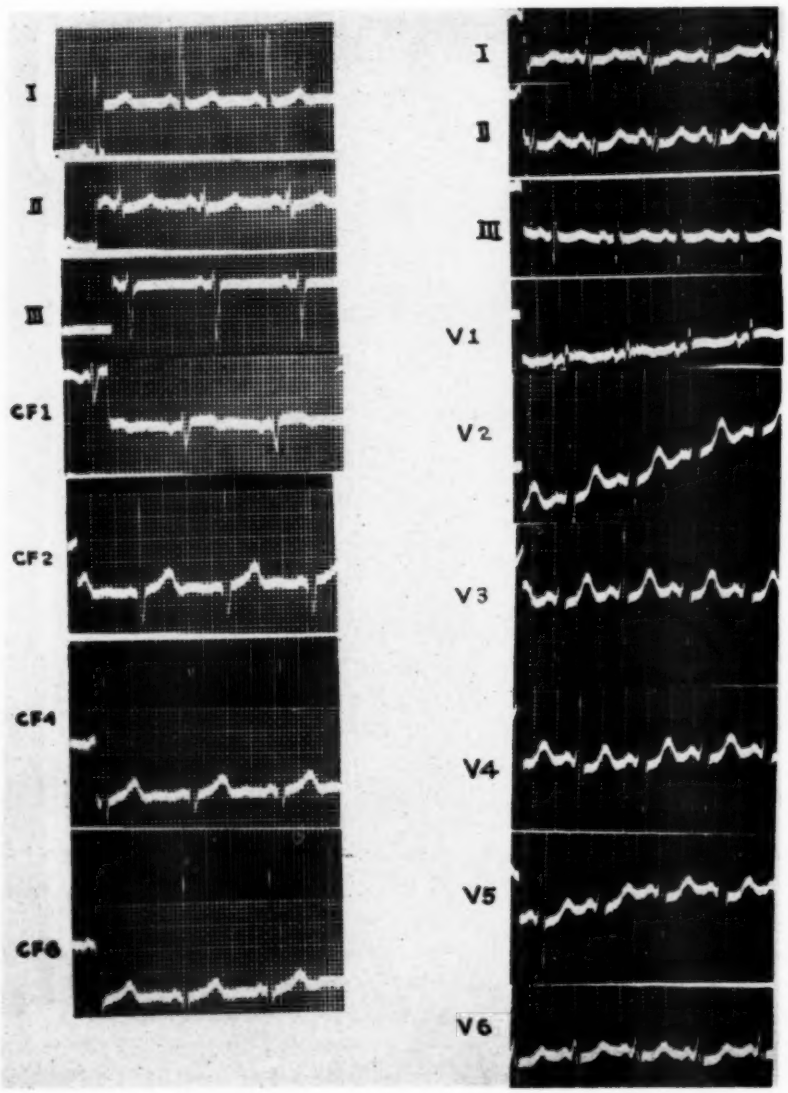

Fig. 18.—Patient F. I. The first tracing (*A*) was taken one year prior to the occurrence of pulmonary embolism and shows left ventricular hypertrophy. The second ECG (*B*), taken twelve hours following pulmonary embolism, reveals the appearance of a large S wave in Leads I, V_5, and V_6 and a relatively high R wave in Leads III and V_1. Necropsy revealed a pulmonary embolus 2.5 cm. above the pulmonary valve. It completely occluded the left main pulmonary artery and partially occluded the right pulmonary artery. No areas of myocardial infarction were found. Right ventricular hypertrophy was not present.

Heart Position

The electrocardiographic picture of a healed posterior myocardial infarct is occasionally difficult to differentiate from a normal tracing in a patient whose heart is in a horizontal, slightly clockwise, rotated position.

SUMMARY AND CONCLUSIONS

Changes in the QRS complexes indicating infarction are of primary importance in obtaining electrocardiographic confirmation of this condition. T-wave and RS-T segment changes alone are not sufficient to indicate the presence of dead cardiac muscle. T-wave inversion alone may merely reflect a stage of ischemia, and RS-T segment changes alone may signify a state of injury; however, unless QRS changes appear, and persist, one is rarely justified in making an electrocardiographic interpretation of myocardial infarction. Experimental production of myocardial infarction[15] has demonstrated the stages through which cardiac muscle passes and the resultant electrocardiographic sequence of changes which correspond to the stages of ischemia, injury, and death of muscle. The latter causes the appearance of permanent Q waves or QS waves over the area of infarction. For Q waves to appear in leads taken over the area of infarction, it is essential that there be living muscle in the ventricular wall opposite, or adjoining, the area of infarction, since the normal sequence of activation in this area is responsible for the genesis of the Q wave. If the infarction involves only the outer portions of the myocardium, or is intramural, a Q wave may not appear, although the QRS configuration will usually be modified.

Routine electrocardiograms should include the three standard leads and at least precordial Leads V_1 through V_6. In patients whose clinical history suggests infarction, if these leads are not confirmatory, additional exploration with other precordial leads should be undertaken. Posterior lesions may show up well in electrocardiograms taken at the ventricular level in the esophagus or in leads taken over the ensiform cartilage. Although a large Q wave in Lead V_F tends to make one suspect a posterior lesion, the presence or absence of such a wave can easily be determined from Leads II and III.[18] Patients without cardiac disease may have a relatively large Q wave in Leads III and V_F due to a horizontal, clockwise rotated, apex forward, heart position. High lateral lesions will be best demonstrated in precordial leads taken over the anterolateral aspects of the third and fourth left intercostal spaces. Serial electrocardiograms furnish valuable information. Whereas changes in a single electrocardiogram may not be confirmatory of a diagnosis of infarction, serial pictures demonstrating a progression of changes may be diagnostic.

The cases presented in this paper demonstrate that an electrocardiogram is still only a laboratory procedure which is an adjunct to the confirmation of a clinical diagnosis of myocardial infarction and should not be relied on completely to establish or disprove a diagnosis of coronary occlusion. Although serial electrocardiographic changes of infarction are highly characteristic, their absence does not rule out a diagnosis of myocardial infarction. Too frequently we have seen a diagnosis of myocardial infarction resting on T-wave changes alone, and

conversely the absence of electrocardiographic changes used as the only negative evidence in ruling out a diagnosis of coronary occlusion in a patient whose history and other laboratory findings were practically diagnostic of myocardial infarction. As has been stated, QRS changes should be present when one makes an electrocardiographic interpretation of myocardial infarction; however, infarction may be present in their absence, so that an electrocardiographic confirmation is impossible. Although most patients with myocardial infarction will have electrocardiograms which will confirm this diagnosis, it is well to remember that occasionally the electrocardiogram will show no characteristic changes in patients with myocardial infarction.

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A CLINICAL STUDY OF 281 AUTOPSY REPORTS ON PATIENTS WITH MYOCARDIAL INFARCTION

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THE autopsies performed at the University Hospitals of Cleveland during the years 1936 through 1945 were reviewed and all reports of myocardial infarction were selected for study. The series is composed of patients whose hearts showed infarction at autopsy, regardless of what the clinical studies had suggested during life. Working from these proved pathological findings an analysis has been made of the clinical observations, laboratory data, and course of each individual patient. This type of approach afforded a unique opportunity for studying such aspects of the problem of coronary disease as incidence, prognosis, accuracy of electrocardiographic diagnosis, cardiac enlargement, and ultimate cause of death.

The recent publication of Wartman and Hellerstein[1] reviewed 2000 autopsies performed at this institution from Jan. 28, 1935, to April 4, 1940. The periods covered by their study and ours overlapped. Their work is a thorough pathological analysis, and furnishes a background for the present study. What autopsy material we have used in this report was analyzed separately, and there is close agreement between the findings in these two reports.

During the ten-year period studied, a total of 3559 autopsies were performed. Of this group myocardial infarction was demonstrated in 281 subjects, an incidence of 7.8 per cent. There were 198 male and 83 female subjects, with a race distribution of 250 white to 31 Negro subjects. To find the sex and race make-up of the total number of autopsies done, we referred to Wartman and Hellerstein[1] who found that 64 per cent of the subjects were male and 36 per cent female, with 80 per cent white and 20 per cent Negro. Thus myocardial infarction in men occurred at a rate of 8.69 per 100 male autopsies and in women at a rate of 6.47 per 100 female autopsies, giving a male to female ratio of 1.32 to 1. Using the same method the white to Negro ratio was 2 to 1.

The average age at death was 61.5 years. For men the average was 60.9 years and for women 62.9 years. The average age at death for the Negroes was 56.1 years as compared with 62.2 years for the white group.

In any discussion of coronary artery disease certain factors which are unrelated to each other, such as family history, occupation, obesity, and the like, are invariably mentioned. Obesity was present in 23 per cent (65 of 279 patients about whom information was available), diabetes mellitus in 14 per cent (37

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of 265 patients), syphilis in 12 per cent (29 of 247), and a history of rheumatic fever, or physical or pathological findings of rheumatic heart disease in 2.7 per cent (7 of 262).

Such information about family history of cardiovascular disease as could be obtained from the hospital records was tabulated. A family history was included in the records of 227 patients. In 154 (68 per cent) a negative family history for heart disease was definitely specified. If all types of cardiovascular disease were considered as a whole, a positive family history was obtained in 73 (32 per cent). In 13 (6 per cent) coronary disease was mentioned specifically.

The occupational histories were reviewed in order to separate the individuals who worked primarily with their hands from those who earned their living principally by executive or professional pursuits. There were approximately equal numbers in these two groups. A group of housewives was dealt with separately and was of about the same size. No particular difference was demonstrated in the age of death beyond that which could be explained by sex differences. The group comprised of those doing manual labor survived for an average of sixty-six weeks after the appearance of symptoms of coronary artery disease, as compared to survival of ninety-one weeks for the executive or professional group. However, such factors as the economic level of the individual and the type of medical care rendered would need to be accurately determined before any definite conclusions could be drawn from these data.

LONGEVITY

One of the many problems presented for solution was that of longevity. Interest was directed to this question since our selection of cases differed from that in the usual clinical reports dealing with coronary disease and angina pectoris.[2-10] This approach included those who die early in the disease when accurate clinical diagnosis is impossible and those whose total course is too short to be included in clinical studies of coronary disease. However, those individuals who have coronary insufficiency but do not at death exhibit an infarct will not be found in this series. Furthermore, this group of individuals who have died with evidence of coronary artery disease should be looked upon as only a special subgroup of a larger number of persons with the same disease, some of whom may still be living. These facts, and the implication that hospitalized patients are usually more seriously ill than nonhospitalized ones, definitely favor a less optimistic view of the problem.

The onset was calculated either from the symptoms of angina pectoris or from evidence of myocardial infarction, whichever appeared first. The average duration of life for the entire group was one and one-half years from the onset of symptoms. Approximately 50 per cent of the patients were dead within two months and 70 per cent within one year. These figures are based on the findings of a selected group of 171 patients (122 male, 49 female) whose histories were adequate to date the onset of symptoms. The percentage of the group surviving at various time intervals after the onset of symptoms is shown in Table I. These data contrast sharply with longevity studies in angina pectoris as can be seen from Table II, and they are difficult to evaluate. They mean, at least, that

the anticipated length of survival of an individual destined to die with a myocardial infarct will follow the pattern outlined by this group.

TABLE I. LENGTH OF SURVIVAL FROM THE FIRST SYMPTOMS OF CORONARY DISEASE (SHOWING THE PERCENTAGE OF PATIENTS WHO WERE STILL ALIVE AFTER VARIOUS TIME INTERVALS)

SURVIVAL TIME	PERCENTAGE OF SURVIVAL	
	MEN (122 SUBJECTS)	WOMEN (49 SUBJECTS)
1 week or less	90.1	77.6
2 weeks	78.7	67.3
3 weeks	72.2	59.2
1 month	63.1	55.1
2 months	53.3	49.0
6 months	43.4	38.8
1 year	31.2	30.6
2 years	20.5	21.0
3 years	15.6	16.6
4 years	10.7	12.5
5 years	6.6	8.2
7 years	0.8	4.1
10 years	0.0	0.0

An effort was made to correlate the age at the time of onset of symptoms with the length of survival afterward in order to draw some conclusions relating to whether younger or older individuals enjoyed the better prognosis. No definite trend could be demonstrated when the ages were grouped by five-year periods (Table III). However, when members of the larger group, whose onsets were below the age of 60 years, were compared with members of the group whose onsets were at the age of 60 or above, the outlook fell from ninety-four weeks for the former to fifty-eight weeks for the latter. These observations are consistent with the usual clinical experiences in dealing with patients of this sort.

CAUSE OF DEATH

The clinical and pathological features of each of the 281 patients with myocardial infarction were considered with the idea of determining the ultimate cause of death. In 149 patients it was possible to date the occurrence of the infarction, and in these the cause of death was tabulated in relation to the duration of life after infarction (Table IV). Among the group who died within one month (ninety-five patients), the most frequent cause of death was congestive heart failure (35 per cent). Two other major causes of death were "sudden unexplained death" (26 per cent), assumed to be due to such mechanisms as ventricular fibrillation or extension of thrombus, and shock (22 per cent) without signs of congestive failure. Relatively infrequently were cardiac rupture (6.3 per cent) and pulmonary infarction (4.2 per cent) the chief causes of death. Among the group who survived longer than one month (54 patients) the most frequent cause of death was a second myocardial infarction (39 per cent), with the only other two significant causes of death being congestive heart failure (20 per cent) and other diseases unrelated to the cardiovascular system (19 per cent).

TABLE II. LONGEVITY IN CORONARY DISEASE (FROM VARIOUS AUTHORS[2-10])

AUTHORS	AVERAGE SURVIVAL IN YEARS
1. Herrick and Nuzum,[2] 1918	
50 patients (dead)	3.0
2. Mackenzie,[3] 1923	
214 patients (dead)	5.4+
3. White,[4] 1926	
66 patients (dead)	3.4
134 patients (living)	4.6
4. White and Bland,[5] 1931	
213 patients (dead)	4.4
273 patients (living)	5.1
5. Eppinger and Levine,[6] 1934	
141 patients (dead)	4.57
6. Wedd and Smith,[7] 1935	
166 patients (dead)	5.8
7. Bland and White,[8] 1941	
171 patients (dead)	3.4
29 patients (living)	12.0
8. Levine and Rosenbaum,[9] 1941	
101 patients (dead)	3.4
271 patients (living)	2.3
9. White, Bland, and Miskall,[10] 1943	
445 patients (dead)	7.9
52 patients (living)	18.4

TABLE III. LENGTH OF SURVIVAL IN WEEKS ACCORDING TO PATIENTS' AGES AT ONSET OF SYMPTOMS

AGE AT ONSET OF SYMPTOMS	NUMBER OF PATIENTS	AVERAGE LENGTH OF SURVIVAL IN WEEKS	AVERAGE LENGTH OF SURVIVAL WHEN ONSET OF SYMPTOMS WAS BELOW AGE 60	AVERAGE LENGTH OF SURVIVAL WHEN ONSET OF SYMPTOMS WAS AGE 60 OR ABOVE
30–34	3	5		
35–39	3	79		
40–44	13	108		
45–49	14	93	93.6 weeks	
50–54	27	69		
55–59	29	120		
60–64	26	75		
65–69	25	63		
70–74	11	70		57.9 weeks
75–79	13	25		
80–84	4	28		
85–89	3	5		

TABLE IV. CAUSE OF DEATH IN PATIENT'S WITH MYOCARDIAL INFARCTION

CAUSE OF DEATH	PATIENTS SURVIVING LESS THAN ONE MONTH	PATIENTS SURVIVING OVER ONE MONTH	PATIENTS WITH UNDETERMINED DATE OF INFARCTION	TOTAL SERIES
Congestive heart failure	33 (34.8%)	11 (20.4%)	33 (25.0%)	77 (27.4%)
Cardiac rupture	6 (6.3%)	2 (3.7%)	1 (0.8%)	9 (3.2%)
Circulatory collapse	21 (22.1%)	0	2 (1.5%)	23 (8.2%)
Sudden unexplained death	25 (26.3%)	3 (5.6%)	9 (6.8%)	37 (13.2%)
Second infarction	0	21 (38.9%)	21 (15.9%)	42 (14.9%)
Pulmonary infarction	4 (4.2%)	2 (3.7%)	6 (4.5%)	12 (4.3%)
Embolic (e. g., brain, extremities, etc.)	1 (1.0%)	1 (1.8%)	6 (4.5%)	8 (2.8%)
Vascular disease (other than coronary artery disease)	3 (3.2%)	3 (5.6%)	20 (15.2%)	26 (9.2%)
Unrelated diseases	1 (1.0%)	10 (18.5%)	33 (25.0%)	44 (15.7%)
Unknown	1 (1.0%)	1 (1.8%)	1 (0.8%)	3 (1.1%)
Totals	95	54	132	281

The frequency with which congestive heart failure appeared as the major cause of death led us to study more closely the administration of digitalis. Because some authors[11-13] recommended caution in the use of digitalis in the presence of acute infarction, we wondered if it was being used as frequently as desirable. Askey and Neurath[11] concluded that the chief danger in the use of digitalis in acute infarction is the increased incidence of thrombo-embolic phenomena. With the almost universally accepted use of anticoagulant therapy in myocardial infarction at the present time, this objection to digitalis therapy is minimized. A selective use of the drug is demonstrated in Table V which shows that 64 per cent of those dying of congestive heart failure were given digitalis as compared to 36 per cent of those dying of other causes. Apparently no evident caution was exercised in the acute stages of infarction, as the same proportion of those dying before one month received digitalis as those dying sometime later.

TABLE V. USE OF DIGITALIS CORRELATED WITH THE CAUSE OF DEATH

CAUSE OF DEATH	PATIENTS SURVIVING LESS THAN ONE MONTH		PATIENTS SURVIVING OVER ONE MONTH		PATIENTS WITH UNDETERMINED DATE OF INFARCTION		TOTAL SERIES	
	NUMBER OF PATIENTS	PERCENTAGE GIVEN DIGITALIS	NUMBER OF PATIENTS	PERCENTAGE GIVEN DIGITALIS	NUMBER OF PATIENTS	PERCENTAGE GIVEN DIGITALIS	NUMBER OF PATIENTS	PERCENTAGE GIVEN DIGITALIS
Congestive heart failure	33	64	11	64	33	64	77	64
Other causes of death	62	39	43	51	99	27	204	36
Totals	95	47	54	54	132	36	281	43

HEART WEIGHT

An ideal opportunity was afforded to study the weights of the hearts accurately and to make some correlation with survival times and with factors assumed to be responsible for cardiac enlargement. The hearts were grouped according to weight and the average length of survival from onset of symptoms determined for each group (Table VI, Column 3). By this method the size of the heart at death and the length of life after the first evidence of the disease could not be correlated.

TABLE VI. CORRELATION OF HEART WEIGHT WITH THE AVERAGE LENGTH OF SURVIVAL, OCCURRENCE OF MULTIPLE INFARCTION, INCIDENCE OF HYPERTENSION, AND THE PRESENCE OF OTHER TYPES OF HEART DISEASE

HEART WEIGHT (GRAMS)	NUMBER OF PATIENTS	SURVIVAL FROM FIRST SYMPTOM		MULTIPLE INFARCTS (PERCENTAGE OF TOTAL PATIENTS)	HYPERTENSION		OTHER HEART DISEASE (AUTOPSY FINDINGS) (PERCENTAGE OF TOTAL PATIENTS)
		NUMBER WITH INFORMATION	AVERAGE SURVIVAL (WEEKS)		NUMBER WITH INFORMATION	PERCENTAGE WITH HYPERTENSION	
100–199	1	1	416	0	1	0	0
200–299	5	1	12	0	5	20	0
300–399	44	30	57	39	43	56	2
400–499	77	52	87	42	70	59	8
500–599	82	48	76	44	76	53	11
600–699	45	23	66	42	44	75	27
700–799	19	12	87	37	19	74	11
800–899	2	1	14	50	2	100	50
Unknown	6	3	78	17	4	50	17
Totals	281	171	77	40	264	60	12

If the occurrence of multiple infarction of the heart is used as a guide to the severity of the coronary artery disease, one might anticipate that the subjects with heavier hearts would have a higher incidence of multiple infarction. This was not found to be the case (Table VI, Column 4).

A study of the relationship of heart size and congestive heart failure was made after those patients with hypertension or other types of heart disease were eliminated from the group. It was found that a direct correlation existed between the size of the heart and the incidence of congestive failure (Table VII). Just as in the entire series, the duration of coronary symptoms and the incidence of multiple infarction did not appear to be related to heart size. However, if the dividing line between normal heart size and cardiac hypertrophy is considered arbitrarily to be 400 grams, then 82 per cent of the entire group, and 74 per cent of the supposedly purely arteriosclerotic group, had cardiac hypertrophy. Even though no correlation was obtained between the incidence of multiple infarction, or the duration of symptoms, and the heart size, we believe that this series supports the premise that coronary sclerosis and myocardial infarction per se may cause enlargement of the heart. This is in agreement with the bulk of evidence in the literature.[14-18]

TABLE VII. CORRELATION OF HEART WEIGHT WITH THE INCIDENCE OF CONGESTIVE HEART FAILURE IN PATIENTS WITHOUT HYPERTENSION OR OTHER TYPES OF HEART DISEASE

HEART WEIGHT (GRAMS)	NUMBER OF PATIENTS	CONGESTIVE HEART FAILURE	
		NUMBER WITH INFORMATION	PERCENTAGE WITH CONGESTIVE FAILURE
100-199	1	1	100
200-299	4	3	0
300-399	19	19	32
400-499	29	25	64
500-599	30	27	70
600-699	7	7	86
700-799	2	2	100
800-899	0	0	0
Unknown	1	1	0
Totals	93	85	59

As would be expected, hypertension and the presence of concomitant heart disease of other types, such as rheumatic, syphilitic, and congenital, were also factors in producing cardiac enlargement. This is shown in Table VI, Columns 5* and 6, where the incidence of these lesions increased as the heart weights increased.

ELECTROCARDIOGRAMS

In 182 subjects electrocardiograms were known to have been taken sometime after the occurrence of infarction. In these subjects we were able to correlate the electrocardiographic interpretation with the post-mortem findings. All the electrocardiographic records included, in addition to the standard leads, at least one chest lead taken at the apex. In the later period of the study multiple precordial leads and augmented limb leads were often used. Many of the infarcts were beyond the acute stage, often by months or years, when electrocardiograms were made or the autopsies performed. Frequently there had been no suspicion during life that coronary disease was present, and in these instances the electrocardiographic observations were not always thorough from the point of view of multiple tracings and additional leads. For these reasons the accuracy of electrocardiographic diagnosis may not appear to be as favorable as in other reports of a similar nature. Feil, Cushing, and Hardesty,[19] in a review of thirty-four patients with recent infarction, found an accuracy of diagnosis of 82 per cent.

Ventricular Infarcts.—In the 182 patients, a definite electrocardiographic diagnosis of myocardial infarction was made 103 times. This diagnosis was found at autopsy to be correct as to location and duration of the injury in 91

*Chi-square analysis of the data of Column 5, Table VI, shows P = 0.061, where P indicates the probability that as much disparity between the observed and theoretical frequencies, or more, could result from random sampling, i. e., the observed results, or worse, would obtain in sixty-one times out of a thousand through chance. This can be taken to mean that the difference observed in this series probably represents a significant deviation.

patients (50 per cent). In 8 additional patients in whom two infarcts were diagnosed from the electrocardiogram, only one infarct was found at autopsy. In the remaining 4 an infarct of the duration specified was present but its anatomical location was incorrect.

In 25 instances changes of the type seen in infarction were present but were not considered sufficiently pronounced to permit a definite diagnosis. In 29 the electrocardiographic patterns were nonspecific in character (such as, negative T waves, low voltage and slurring of the QRS complexes, and marked left axis deviation) and of the type often referred to as indicating "myocardial damage." Ten examples of left bundle branch block were found and, owing to this aberrant ventricular excitation, an electrocardiographic diagnosis of infarction could not be made. In 13 patients the only abnormality was that of rhythm (in 9 there was auricular fibrillation) and in 2* the electrocardiograms were considered to be normal. This is summarized in Table VIII.

TABLE VIII. ELECTROCARDIOGRAPHIC FINDINGS IN 182 SUBJECTS WITH AUTOPSY DIAGNOSIS OF MYOCARDIAL INFARCTION

ELECTROCARDIOGRAPHIC FINDINGS	NUMBER OF SUBJECTS	AUTOPSY FINDINGS	
		CORRECT AS TO DURATION	CORRECT AS TO LOCATION
Recent anterior infarction	55	55	53
Old anterior infarction	6	6	6
Recent posterior infarction	22	22	21
Old posterior infarction	6	6	5
Recent auricular infarction	2	2	2
More than one infarct	12	12	4
Suggestive of infarction	25		
"Myocardial damage"	29		
Left bundle branch block	10		
Abnormal rhythm (only abnormality)	13		
Normal	2		
Totals	182	103	91

These data indicate that when the electrocardiogram shows the well-developed and conventional pattern of infarction the diagnosis is almost always correct. Infarction is often found at autopsy when the electrocardiogram is considered to be only suggestive of infarction or when it shows other abnormal but nonspecific changes. It should be made clear that for the most part the electrocardiographic interpretations used in this analysis were those recorded at the time the record was taken. If the electrocardiograms were reviewed in the light of present-day knowledge, and if the additional leads used routinely in this laboratory today had then been available, it is reasonable to assume that

*One was a 57-year-old white man who died suddenly while in the hospital for treatment of gangrene of the heel. The autopsy showed only small areas of fibrosis in the septum and posterior wall of the left ventricle, the largest only 8 mm. in diameter. The other was a white man, aged 62, who died postoperatively, and the autopsy showed a 4- by 4-cm. healed transmural infarct in the midportion of the anterior wall of the left ventricle. Only one chest lead had been taken (CR_4).

some of the subjects would be removed from the "suggestive" or "nonspecific" group and correctly placed among those in whom the diagnosis was accurately made.

Finally, it should be emphasized that a completely normal electrocardiogram is seldom found (in our series, only twice in 182 patients) in the presence of proved myocardial infarction.

Auricular Infarcts.—The patients who showed an abnormality of auricular impulse formation were considered to determine whether this disturbance could be used to support the diagnosis of infarction of the auricles. Auricular infarction occurred 24 times in 281 autopsy subjects, an incidence of 8.5 per cent. This is similar to that reported by Wartman and Hellerstein[1] who found the incidence of atrial infarction to be 7.2 per cent, but is lower than the incidence of 17 per cent reported by Cushing, Feil, Stanton, and Wartman.[20] These three studies were done at the same institution and overlap in time to some extent. The difference in incidence probably occurred because during the different years covered by these studies there was not a consistent search made for atrial infarction at autopsy.

In 17 of the 24 patients with auricular infarction the process was recent, but electrocardiograms were taken subsequent to the infarction in only ten. Six of these 10 patients (60 per cent) had abnormal auricular impulse formation (1 with sinus bradycardia and ventricular escape, 1 with nodal rhythm, and 3 with auricular fibrillation). This type of approach was used by Cushing, Feil, Stanton, and Wartman[20] when they reviewed subjects showing auricular infarction at autopsy, and found that 74 per cent of them had had abnormal auricular mechanisms during life.

From the clinical point of view, the usual way to study a problem of this sort is to begin with the electrocardiographic findings and look to the pathological material for confirmation. In this series 107 patients had electrocardiograms taken soon after the occurrence of ventricular infarction. Twenty-seven of them showed abnormal auricular rhythm (fibrillation, flutter, paroxysmal auricular tachycardia, nodal rhythm, parasystolic rhythm, and sinus bradycardia with ventricular escape), but only 6 (22 per cent) of these patients had auricular infarction at the time of autopsy. The proportion remained the same when auricular fibrillation alone was considered as evidence for auricular infarction (4 of 18, or 22 per cent). This figure is probably even smaller since in a few patients the auricular arrhythmia may have been present before they had the infarct. Auricular infarction occurred only 4 times in 80 patients with normal auricular rhythm (5 per cent). The chances are only 156 in 10,000 that as great a difference as between 5 and 22 per cent could arise by chance alone in samples of this size. Therefore the chances of finding auricular infarction at autopsy are greatest in those patients who have abnormal auricular rhythm clinically. At the same time, since only 22 per cent of patients with abnormal auricular rhythm in the electrocardiogram are found to have an auricular infarct, one is not on firm ground when suggesting such infarction from the electrocardiogram.

SUMMARY

1. A study was made of 281 patients with myocardial infarction found in reports of 3559 autopsies performed during the ten-year period 1936 through 1945. This was an incidence of 7.8 per cent.

2. The average survival after the appearance of symptoms of coronary artery disease was one and one-half years for the group.

3. The patients who were less than 60 years of age at the onset of their symptoms survived for an average of ninety-four weeks, compared to an average of fifty-eight weeks survival for patients whose symptoms began after the age of 60.

4. The most frequent cause of death in patients who died within one month after infarction was congestive heart failure. In the group who survived longer than one month, death was most commonly caused by a second myocardial infarct.

5. Coronary arteriosclerosis and myocardial infarction were found to be causative agents in cardiac hypertrophy, even in the absence of hypertension and other types of heart disease.

6. Electrocardiograms were taken after infarction in 182 patients. A positive diagnosis of infarction was made in 103 (57 per cent) and the electrocardiogram was suggestive in 25 others (14 per cent). In only 2 patients was the electrocardiogram normal.

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THE EFFECT OF THE LEVEL OF THE LIGATURE ON MORTALITY FOLLOWING LIGATION OF THE CIRCUMFLEX CORONARY ARTERY IN THE DOG

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ONE useful approach to the problem of coronary occlusion is to determine the effect of various drugs and procedures on the incidence of arrhythmias and mortality in experimental animals in which coronary vessels have been occluded. Early in the course of an experiment of this type, it was suspected that the precise level of the ligature placed about the circumflex branch of the left coronary artery in dogs influenced the mortality. An examination of the literature revealed that this factor had neither been investigated nor controlled by previous workers. In fact, mortality rates reported for this procedure by various authors[1-7] varied from 0 to 100 per cent, a range betraying failure to control all significant factors. Since mortality experiments at best are extravagant of animals, it is important, if statistically significant results are to be obtained, that advantage be taken of every means of securing uniform results. Accordingly, the present experiments were undertaken to determine the effect of the precise level of the ligature on mortality in dogs following ligation of the circumflex branch of the left coronary artery.

METHODS

Seventy-five young adult dogs weighing between thirteen and twenty-six pounds were used. Under intravenous pentrobarbital sodium anesthesia, and with artificial respiration, the chest was opened through the fourth left intercostal space under aseptic precautions. The pericardium was opened, and the bifurcation of the left coronary artery identified when it could be visualized. The circumflex branch of the left coronary artery was isolated, and a linen ligature was passed beneath it, utilizing a ligature carrier which allowed for a minimum of tension or torsion to the vessel. A loose surgeon's knot was placed in the ligature, and the ends were led from the chest at the extremities of the incision. Sufficient slack was allowed to prevent tension on the ligature due to expansion of the lungs. In some animals, the ligature was placed at the origin of the circumflex branch, in others at a point approximately 5.0 mm. distal to the bifurcation of the left coronary artery, while in other animals the point chosen was approximately 10 mm. distal to the bifurcation. The pericardium was then approximated, and the chest closed. Postoperatively 15 to 20 c.c. of physiological

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saline per kilogram of body weight were given subcutaneously. The next day, eighteen to twenty-four hours after placement of the ligature, occlusion of the circumflex branch of the left coronary artery was effected in the conscious animal by traction on the protruding ends of the ligature. The animals were observed continuously for one hour following occlusion, and at intervals for twenty-four hours thereafter.

Electrocardiograms (Leads I, II, and III) were recorded from each animal before operation and immediately before occlusion. This established the absence of electrocardiographic evidence of damage due to the operative trauma. Lead II was recorded continuously during occlusion and at frequent intervals during the one-hour observation period. Five animals were eliminated from the series because of electrocardiographic evidence that the ligature had prematurely occluded the coronary vessel.[3,7-11]

All animals were necropsied, the survivors after sacrifice at twenty-four hours. The heart was excised and weighed after removal of the pericardium, evacuation of the clots, trimming of the large vessels, and washing. The distance of the ligature from the bifurcation of the left coronary artery was carefully measured, since it was early discovered that the distance as estimated at operation was subject to gross error. The left coronary artery was then cannulated from the aorta, the circumflex branch was sectioned just distal to the ligature, and the system subjected to a pressure equivalent to 150 mm. of mercury, using as perfusing mediums water, citrated blood, or in a few cases, Schlesinger's mixture.[12] By this means, the efficacy of the ligature was demonstrated beyond doubt. This was considered important in view of the demonstration by Blumgart and co-workers[10] and others[9,13,14] that ventricular fibrillation and death may occur within a few seconds after re-establishment of blood flow following occlusion. The circumflex branch of the left coronary artery was then dissected more completely, the ventricular branches arising from it were located, and their distances from the origin measured. Two animals were discarded because the ligature had torn the coronary vessel and hemorrhage had resulted; one other animal was discarded because accidental injury to the excised heart prevented identification of vascular branches.

RESULTS

Of the sixty-seven acceptable animals, twenty-one (31 per cent) died within fifteen minutes following occlusion of the circumflex branch of the left coronary artery; in each of these there was electrocardiographic evidence of ventricular fibrillation. An additional seventeen dogs (25 per cent) died after one hour, but within twenty-four hours following occlusion, of causes not specifically identified. The total twenty-four-hour mortality was, therefore, thirty-eight animals (57 per cent).

Table I presents the data regarding the effect of the level of the ligature on the one-hour (ventricular fibrillation) and twenty-four-hour mortalities. In the upper part of the table, the animals have been grouped according to the number of ventricular branches which at autopsy were found between the true origin of the circumflex and the ligature, and which therefore escaped occlusion. It

is apparent that both the one-hour and twenty-four-hour mortalities were appreciably higher when all branches were occluded than when one or more of the first tiny branches were left free. For one-hour mortality, the extremes are 59 and 16 per cent, and for twenty-four-hour mortality, 82 and 36 per cent. A chi square statistical analysis showed these differences to be significant.

TABLE I. EFFECT OF THE LEVEL OF THE LIGATURE ON MORTALITY

LEVEL OF LIGATURE	NUMBER OF DOGS	ONE-HOUR MORTALITY (PER CENT)	24-HOUR MORTALITY (PER CENT)
1. Number of unoccluded branches proximal to ligature			
0	22	59	82
1	19	16	47
2	15	20	47
3–4	11	18	36
Totals	67	31.3	56.7
2. Distance (mm.) from origin to ligature			
0–3	19	58	84
4–6	23	17	57
7–10	13	23	30
11–14	12	25	42
Totals	67	31.3	56.7

In the second part of the table the animals have been grouped according to linear distance in millimeters between the exact origin of the circumflex and the ligature. Again it is clear that the closer the ligature is to the origin, the higher is the resulting mortality. Even a displacement of 3.0 mm. alters the mortality, undoubtedly because of the occasional small branches thus left free.

Of the sixty-seven animals, thirty-six were males and thirty-one females. The one-hour and twenty-four-hour mortalities for males were 33 and 61 per cent, and for females 29 and 52 per cent. Since no relationship between sex and the level of the ligature could be disclosed, these data indicate the lack of any significant sex difference in response to ligation.

DISCUSSION

The present results indicate that the precise level of the ligature significantly influences the incidence of ventricular fibrillation and fatality produced by ligation of the circumflex branch of the left coronary artery in dogs. This factor undoubtedly contributes to the nonrandom differences in mortality reported by different workers, as mentioned in the introduction. In many instances there is no indication that special care was exercised in locating the ligature; in other instances the ligature was stated to have been placed within 1.0 to 2.0 cm. of the origin, a range yielding a low and possibly variable mortality. This factor must be carefully controlled in any future experiments designed to determine the effect of therapeutic or experimental procedures on the course of events in this type of coronary occlusion. Ligation at the true origin is preferable, since the resulting

one-hour mortality of around 50 per cent permits the demonstration of either beneficial or deleterious effects.

Wood and Wolferth[11] have suggested that perhaps the circumflex branch supplies a region of the heart which, when deprived of its blood supply, is peculiarly prone to give rise to ventricular fibrillation. On the other hand, the marked effect of excluding even a small branch from the ligature implies either that the ligated animal is so delicately balanced between life and death that a small change in the area of infarction can tip the balance one way or the other, or, that the particular area supplied by these initial branches is vital for cardiac function.

In the course of this work a careful analysis was made of all reports concerning mortality in the dog following ligation of various coronary arteries and their branches. The combined data are presented in Table II, together with Wigger's[15] estimates of the percentage of the total blood flow to the heart carried by these vessels. For the circumflex branch, the literature shows average mortalities of 43 per cent in one hour and 59 per cent in twenty-four hours; this compares with the present results of 31 per cent and 57 per cent, neglecting the level of the ligature. If the ligature is precisely placed at the true origin of the circumflex, the mortalities are higher, namely, 59 and 82 per cent.

TABLE II. MORTALITY FOLLOWING LIGATION OF VARIOUS CORONARY VESSELS IN THE DOG

VESSEL LIGATED	MORTALITY				BLOOD FLOW PER CENT OF TOTAL
	ONE HOUR		24-HOUR		
	NUMBER OF DOGS	PER CENT MORTALITY	NUMBER OF DOGS	PER CENT MORTALITY	
Both left and right coronary arteries[16,17]	7	100	7	100	100
Left coronary artery[4,5,18,19]	38	100	38	100	80
Circumflex branch[1-7]	87	43	102	59	50
Anterior descending branch[3-7,20-27]	261	28	193	46	30
Right coronary artery[4-7,28,29]	39	10	25	40	20

SUMMARY AND CONCLUSIONS

1. In sixty-seven dogs a loose ligature was placed about the circumflex branch of the left coronary artery, and twenty-four hours later, without anesthesia, the vessel was occluded by traction on the ligature.

2. In twenty-two animals in which autopsy established the ligature to be located at the true origin of the circumflex branch, the one-hour mortality (due to ventricular fibrillation) was 59 per cent, and the twenty-four-hour mortality was 82 per cent.

3. In the remaining forty-five animals in which one or more small initial sub-branch of the circumflex was not included in the ligature, the respective mortalities were 18 and 44 per cent.

4. Small differences in the level of the ligature therefore significantly influence mortality; this factor must be carefully controlled in future experiments designed to determine the effect of therapeutic or experimental procedures on this type of coronary occlusion.

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THE EFFECT OF QUINIDINE ON VENTRICULAR FIBRILLATION INDUCED BY CORONARY LIGATION

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NUMEROUS attempts have been made in the field of animal experimentation to support the use of quinidine in clinical coronary occlusion as a prophylatic agent against possible ventricular fibrillation. Quinidine has been reported to be effective in raising the "fibrillation threshold" following electrical stimulation of the ventricles in living animals,[1-6] after electrical stimulation of an isolated frog heart,[7] in isolated hearts perfused with toxic drugs,[8,9] following hydrocarbon inhalation and epinephrine injection,[10,11] and in dogs treated with toxic drugs.[12] None of these methods, however, would appear to simulate the ischemic mechanism which presumably is responsible for ventricular fibrillation in clinical coronary insufficiency. Only two reports were found in which coronary artery ligation was employed to produce this arrhythmia. Moisset de Espanes[13] reported that quinidine increased the incidence of fibrillation from 60 per cent in twenty-five control dogs to 80 per cent in twenty-five treated dogs. Smith, McEachern, and Hall,[14] on the other hand, reported that quinidine lowered the twenty-four-hour mortality from 70 per cent in sixteen control dogs to 55 per cent in twenty treated dogs. Neither of these apparently contradictory results, however, proved to be statistically significant.

The purpose of the present experiment was to determine the effect of quinidine on the incidence of ventricular fibrillation induced in dogs by ligation at the origin of the circumflex branch of the left coronary artery, utilizing previous information regarding the importance of accurate localization of the ligature.[15]

METHOD

The experimental procedure employed was essentially that of Smith and associates.[14] Fifty young adult dogs weighing between 5.7 and 11.4 kilograms were used. Under Nembutal anesthesia and artificial respiration, the thorax was opened in the fourth left intercostal space; the pericardium incised; and the origin of the circumflex branch of the left coronary artery was freed by careful dissection. A loose ligature was then placed about the origin of the vessel proximal to any subbranches regardless of size. This was considered important since preceding experiments[15] had shown that the mortality rate is influenced by the precise location of the ligature. The free ends of the ligature were led out of the thorax through the surgical wound, leaving sufficient slack within to prevent accidental tightening of the loosely tied knot. The pericardium and the chest wall were then closed and the dog allowed to recover. On the following day (twenty to thirty hours later) the dog was suitably restrained on a padded dog

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board, and coronary occlusion accomplished in the conscious animal by traction on the free ends of the ligature.

Treated dogs received quinidine sulfate in doses of 10 or 20 mg. per kilogram of body weight. Each dose was dissolved in 60 c.c. of saline solution and administered intravenously over a period of twenty minutes from a graduated burette. Five minutes after completion of the infusion, the coronary artery was occluded.

Electrocardiograms were taken before the initial surgery, and before, during, and at intervals for one hour after vessel occlusion. In all cases, characteristic T-wave and RS-T segment changes immediately following ligature traction established the fact that effective occlusion occurred at this time and not before. If death occurred within the first hour, its time and cause were established by the electrocardiogram and immediate autopsy. After the first hour the surviving animals were returned to their cages and observed at intervals to establish the approximate time of death, while those surviving twenty-four hours were sacrificed. Autopsies were performed on all dogs to establish the proper location and security of the ligature, and to rule out hemorrhage or serious infection as an accidental or contributory cause of death.

RESULTS

Table I presents mortality rates for twenty-one untreated animals, seventeen treated with quinidine sulfate, 10 mg. per kilogram, and twelve treated with 20 mg. per kilogram of body weight. The fifteen-minute mortality represents thirty-five deaths within this period following vessel occlusion; thirty-three died of ventricular fibrillation and two of asystole. Both dogs dying of asystole received quinidine sulfate, 20 mg. per kilogram. It is apparent that quinidine provided no protection from immediate death, for the control mortality rate of 57 per cent was increased to 65 per cent and 100 per cent by the smaller and larger doses of quinidine, respectively. It is probable that the larger dose of quinidine contributed to the fatal effects, for the 100 per cent mortality is significantly greater (at the 2 per cent level) than the control mortality of 57 per cent.

TABLE I. MORTALITY FOLLOWING EXPERIMENTAL CORONARY LIGATION

	TOTAL DOGS	MORTALITY					
		WITHIN 15 MINUTES		WITHIN 5 HOURS		WITHIN 24 HOURS	
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Control	21	12	57	14	67	17	81
Quinidine 10 mg. per kg.	17	11	65	11	65	15	88
Quinidine 20 mg. per kg.	12	12*	100	12	100	12	100

*Of these twelve dogs, ten died of ventricular fibrillation, and two of asystole.

Table I also includes five-hour and twenty-four-hour mortality rates. The former represents deaths during the period in which the quinidine was estimated to exert a pharmacological effect. It is apparent again that the quinidine increased rather than decreased the mortality rate, although the differences are not statistically significant.

DISCUSSION

The results obtained in fifty dogs indicated that quinidine did not exert a favorable effect upon ventricular fibrillation or other cause of death produced by coronary artery occlusion in the dog. The results, in fact, suggest that quinidine increases mortality. The two deaths from asystole in the dogs receiving the larger dose of quinidine may possibly have been a manifestation of quinidine poisoning, since toxic doses of the drug have been shown to produce all forms of heart block and cardiac arrest.[16-19]

The doses of quinidine used in this study (10 and 20 mg. per kilogram intravenously over a twenty-minute period) were intermediate with respect to doses previously employed experimentally. Smith and associates[14] reported favorable results with 32.5 mg. per kilogram injected "slowly." Judging from the convulsions, nausea, and vomiting which they reported, their dose was excessive or injected too rapidly. Most of the quinidinized animals in the present investigation manifested salivation, ataxia, and a sufficient degree of apathy to render accurate evaluation of pain during and following vessel occlusion impossible. Whether smaller does would have shown a favorable effect on mortality is not known.

Differences in operative technic, ligature location, and methods of drug administration make comparison of similar studies difficult at best. Establishment of a single standardized technic for coronary artery occlusion, with or without drug administration, would prove a great help in comparing and analyzing experimental results in the future.

That the available experimental evidence supports the clinical use of quinidine in acute coronary insufficiency is questioned. The reports indicating a favorable effect of quinidine on ventricular fibrillation are based upon experimental procedures which do not simulate the ischemic mechanism believed to initiate the arrhythmia following coronary occlusion. On the other hand, the results reported by investigators employing coronary artery ligation methods, including the present data, suggest a harmful rather than a beneficial effect.

SUMMARY AND CONCLUSIONS

1. Under Nembutal anesthesia, loose ligatures were placed around the origin of the circumflex branch of the left coronary artery, the free ends brought to the outside, and the surgical incision closed. The next day, without anesthesia, the artery was occluded by traction on the free ends of the ligature and the response of the animal was followed for twenty-four hours.

2. Of twenty-one control animals, 12 or 57 per cent died of ventricular fibrillation within fifteen minutes, and five or 24 per cent died of unknown cause between one and twenty-four hours.

3. Of seventeen similar animals given 10 milligrams per kilogram of body weight of quinidine sulfate intravenously over a period of twenty minutes prior to vessel occlusion, eleven or 65 per cent died of ventricular fibrillation within fifteen minutes, and four or 23 per cent died of unknown cause between one and twenty-four hours.

4. Of twelve animals treated similarly with quinidine in doses of 20 milligrams per kilogram of body weight, all died within fifteen minutes: ten died of ventricular fibrillation and two of cardiac arrest.

5. Although the mortality rate was increased following quinidine administration, the increase was statistically significant only in the case of the fifteen-minute mortality with the higher dosage of quinidine.

6. These results provide no support for the belief that quinidine protects against ventricular fibrillation induced by acute coronary insufficiency.

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MULTIPLE PREGNANCIES IN PATIENTS WITH RHEUMATIC OR CONGENITAL HEART DISEASE

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SINCE the studies of Angus MacDonald[1] in 1878, there has been considerable interest in the ability of women with heart disease to withstand the added burden of pregnancy. Mackenzie[2] reported that the evaluation of the patient's tolerance for actual work was an important guide in assessing the ability of that patient to meet the requirements of pregnancy and labor. In their reviews of the more recent literature Jensen[3] and Bunim and Rubicius[4] have studied the relationship of heart disease to maternal mortality and the development of congestive heart failure during pregnancy and the puerperium. Bunim and Rubicius expressed the belief that the prognosis of the cardiac patient during pregnancy is determined best by considering that patient's position in the natural history of her rheumatic heart disease, as described by Cohn and Lingg.[5,6] These workers felt further that such an assay is more inclusive than the practice proposed by Hamilton and Thomson[7] of evaluating the factors which serve to classify patients into *favorable* and *unfavorable* groups. It must be pointed out, however, that the features which characterize the cardiac patients of the unfavorable category are the major clinical criteria of rheumatic heart disease in its later phases and that these features serve as a simple guide to the recognition of such stages of the disease. The use of the classification advocated by Hamilton and Thomson[7] has led to the development of methods of management of cardiac patients during pregnancy by which the mortality of the so-called favorable group has been reduced to a level no greater than the mortality in a similar group of nonpregnant cardiac patients.[8] Hamilton and Thomson designate as unfavorable those patients with signs or history of heart failure, a dangerous disorder of the heart beat, such as auricular fibrillation, or other complicating serious disease. The maternal mortality in the unfavorable group is 16.7 per cent as contrasted with 2.3 per cent in the favorable group, those patients with heart disease in whom the listed features are absent.

The majority of the previous reports have indicated that parity per se has relatively little effect on the ultimate prognosis in women with heart disease.[3,4,7] Reid[9] found that patients with heart disease who completed five or more pregnancies died at an average age which was only slightly less than that of a corresponding group of nulliparous cardiac patients. Boyer and Nadas[10] also were unable to demonstrate that pregnancy resulted in any significant shortening of

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life in women with cardiac disorders. Cohn and Lingg[5] reported a duration of life which was practically identical in men and in women with rheumatic heart disease. Furthermore, it has been reported[1] that unpublished data of Cohn and Lingg have shown that in a carefully controlled series of 169 cardiac patients with one or more children, there was no significant difference in the clinical course, the time of onset of congestive failure, the duration of life after onset of the heart disease, or the age at death, when they were contrasted with 215 nulliparous women with heart disease of similar degree. These earlier reports suggest that it is the extent of the cardiac damage, rather than the cardiac abnormality alone, which is the important factor in determining the risk of pregnancy. The opinion is still held in some quarters, however, that multiple pregnancies are hazardous and to be avoided in any woman with heart disease, and that this is true regardless of the degree of compensation. Apparently, this view rests upon the belief that the additional load imposed upon the diseased heart by the pregnancy increases the permanent cardiac damage. There has been relatively little evidence to support this view, but, on the other hand, it has not been refuted completely because the number of patients with heart disease who have had multiple pregnancies and who have been observed as regards their subsequent course is as yet insufficient.

In order to determine why certain women with heart disease tolerate multiple pregnancies with seeming ease and to observe the late effects of childbearing upon cardiac disorders, we have collected data from fifty-two women with rheumatic heart disease and one woman with a congenital cardiac anomaly who completed four or more pregnancies to full term or at least through the second trimester. The data were drawn from a review of the records in the clinic, the hospital, and the social service department. All of the patients who were living at the time of this study were interviewed at length and re-examined. The review included inquiry into the nature of the attacks of acute rheumatic fever, the duration of the heart disease, the age at the time of the various pregnancies, the manifestations of cardiac embarrassment during the pregnancies, the maternal mortality, the chronologic development of evidence of heart failure, the factors contributing to impairment of cardiac function, and finally the duration of life and the cause of death. The clinical cardiac diagnosis was made in the usual manner, supplemented by radiographic and electrocardiographic studies.

RESULTS

A total of fifty-three patients was studied. Thirty patients had died. All of the twenty-three individuals who were living were re-examined and re-evaluated by us. Four of these women died while this study was being completed.

Post-mortem examination, confirming the major clinical diagnoses, was performed in twenty-nine (85.3 per cent) of the thirty-four patients who died. The incidence of the various types of valvular disease in the entire group and in those individuals who were subjected to autopsy study is shown in Table I. Patients with syphilitic heart disease as the sole cardiac diagnosis were not included because of the uncertainty as to the time of onset of cardiac involvement in relation to the pregnancies. In the entire group, disease of the mitral valve

alone occurred in twenty-nine subjects (54.7 per cent); both the mitral and aortic valves were involved in fifteen patients (28.3 per cent); there was mitral valvular disease complicated by hypertension (six patients) or by hypertension and syphilitic aortic insufficiency (two patients) in eight patients (15.1 per cent). In a single instance (1.9 per cent) there was congenital heart disease alone. The distribution of the various disorders is much the same for the autopsied series as for the entire group. The incidence of the various types of valvular disease was not unusual with the possible exception that in no instance was the deformity confined to the aortic valve alone. The extent of the valvular damage and the degree of cardiac hypertrophy encountered in the twenty-nine patients subjected to autopsy was usual for such studies and indicated that the cardiac disease present at the time of death was of major degree. The weight of the heart was recorded in fourteen of the autopsies. The average weight of the heart was 408 grams with a range of 250 to 695 grams. In only a single instance was the weight of the heart less than 300 grams; this heart was from a woman, aged 26 years, who died of septicemia secondary to a criminal abortion. We consider these findings of considerable significance and evidence against the belief that multiple pregnancies in a woman with heart disease suggest that a minimal anatomic cardiac disorder is present.

TABLE I. INCIDENCE OF VARIOUS TYPES OF VALVULAR DISEASE IN THE ENTIRE GROUP AND IN SUBJECTS EXAMINED POST MORTEM

ANATOMIC DIAGNOSIS	ENTIRE GROUP		POST MORTEM SUBJECTS	
	NUMBER	PER CENT	NUMBER	PER CENT
1. Mitral valvular disease	29	54.7	13	44.8
2. Mitral and aortic valvular disease	15	28.3	11	38.0
3. Mitral valvular disease and hypertension	8	15.1	4	13.8
4. Congenital heart disease	1	1.9	1	3.4
Totals	53		29	

The single instance of congenital heart disease was unusual in many respects. This patient died of congestive heart failure at the age of 64 years. She had survived ten pregnancies without significant cardiac embarrassment, the last one at the age of 30 years. Massive dilatation of the major branches of the pulmonary arteries was demonstrated radiographically twelve years before her death. This was confirmed by angiocardiography (Dr. J. L. Marks) eight months prior to death; this study also disclosed complete calcific thrombosis of the right main pulmonary artery. The post-mortem examination revealed diffuse dilatation of the entire pulmonary arterial tree with tremendous aneurysmal dilatation of the pulmonary artery.

The fifty-three patients in this series had a total of 364 pregnancies or an average of nearly seven (6.87) per patient. The distribution of pregnancies per patient is shown in Table II. Because of the manner of selection of the cases,

all patients had four or more pregnancies carried through to delivery or at least through the second trimester. The number ranged up to a maximum of sixteen in one instance. We have been unable to demonstrate any correlation between the severity of the cardiac disturbance, as shown by post-mortem examination, and the number of pregnancies. The records and observations made at the time of the pregnancy were incomplete in the majority of the cases and we were therefore unable to learn if any relation existed between the degree of cardiac damage present at that time and the course or occurrence of the pregnancies. Therefore, while all of these women had valvular damage of at least average degree when they died or when they were re-examined by us, we have insufficient objective evidence to state with certainty their position in the natural history of rheumatic heart disease at the time when the pregnancies occurred.

TABLE II. DISTRIBUTION OF PREGNANCIES PER PATIENT

NUMBER OF PREGNANCIES	NUMBER OF PATIENTS	TOTAL PREGNANCIES
16	1	16
12	1	12
11	2	22
10	6	60
9	3	27
8	9	72
7	5	35
6	4	24
5	8	40
4	14	56
Total	53	364

MATERNAL MORTALITY

There were five deaths during the 364 pregnancies, a maternal mortality of 1.3 per cent per pregnancy. In only one instance was the fatal outcome related to congestive heart failure. Two deaths were caused by peritonitis resulting from self-induced abortions. The third fatality was due to acute bacterial endocarditis secondary to a peritonsillar abscess and another resulted from generalized septicemia which was secondary to erysipelas. The final death occurred from a cerebral embolus which followed a therapeutic abortion performed in a patient with congestive heart failure, auricular fibrillation, and repeated peripheral and cerebral embolization. An effort was made to classify these patients at the time of each pregnancy according to the criteria of Hamilton and Thomson. If congestive failure developed during any pregnancy, that patient was classed as unfavorable for all succeeding pregnancies. When grouped in this manner forty-one patients (77.4 per cent) fell into the favorable category in each pregnancy and twelve patients (22.6 per cent) fell into the unfavorable group during one or more pregnancies. The mortality for these patients was 1.2 per cent and 2.0 per cent respectively in contrast with 2.3 per cent and 16.7 per cent in the experience of Hamilton and Thomson.[7,8] The annual death rate for nonpregnant women with rheumatic heart disease between the ages of 20 and 40 years has been

reported as 2.5 per cent, and for all women in that age group it is 0.4 per cent.[8] Consequently the mortality rates in our series are surprisingly low. This may be due to the relatively small series of cases and in part to the manner of selection of patients. The surviving patients were selected as they came into the cardiac clinic; in many instances this was some years after the childbearing period. The patients who had died were selected only if it was felt that adequate information was available in their records to meet the purposes of this study.

CONGESTIVE HEART FAILURE

Congestive heart failure* apparently resulting from the burden of the pregnancy superimposed upon the underlying heart disease occurred in fifteen of the fifty-three patients (28.3 per cent) or in forty-one of the total of 364 pregnancies (11.3 per cent). This latter figure compares favorably with that of 14 per cent observed by Bunim and Rubicius[4] and that of 20 per cent reported by Hamilton and Thomson.[7] Our lower figure is no doubt due in part to the fact that we are dealing with a special group, that is, women who were able to tolerate four or more pregnancies. Consequently those individuals with heart disease of such severity that they were inclined to undertake, or whose physicians permitted, fewer than four pregnancies are excluded from our observations.

In Table III the fifteen patients who developed congestive heart failure have been arranged in decreasing order of number of pregnancies. Something of the pattern of the multiple pregnancies in each patient is shown in that the time at which heart failure occurred, if it appeared, is indicated in every instance. In three patients (Patients 4, 34, and 36) cardiac failure occurred during every pregnancy, whereas in three others (Patients 27, 32, and 42) it did not appear until the final confinement. There were four individuals (Patients 1, 5, 19, and 38) who developed cardiac decompensation during their initial pregnancies, but who did not have failure in at least some of the subsequent pregnancies. This is against the rule, however, for in addition to the three women who had heart failure with every pregnancy, there were five others who had heart failure with all succeeding pregnancies once cardiac decompensation appeared. Thus it may be said that in this group, once congestive failure occurred during pregnancy, there was a 53.3 per cent likelihood that it would develop in subsequent pregnancies. There was a distinct tendency for congestive failure to appear earlier and earlier with each succeeding pregnancy (see Cases 26 and 34) but there were numerous exceptions to this rule. In only six of the 364 pregnancies was auricular fibrillation associated with heart failure.

There is general agreement that rheumatic exacerbations are unusual during pregnancy. This is especially true in women past the age of 20 years. In no patient in this group did the congestive failure appear to be related to a recognizable recurrence of active rheumatic fever.

*The criteria used for the diagnosis of congestive heart failure were râles at the bases of the lungs, and heptomegaly in those patients whose records were available to us, or a history of orthopnea, paroxysmal dyspnea, or cardiac pain of sufficient degree to require complete rest. While these criteria may be open to some criticism, we feel they are reliable in view of the careful questioning and the comparison of the symptoms with those during other pregnancies and those during subsequent episodes of cardiac decompensation.

TABLE III. ANALYSIS OF FIFTEEN PATIENTS IN WHOM CONGESTIVE FAILURE COMPLICATED ONE OR MORE PREGNANCIES

PATIENT NUMBER	DIAGNOSIS	TOTAL PREGNANCIES	INDIVIDUAL PREGNANCY NUMBER										
			1	2	3	4	5	6	7	8	9	10	11
38	M.V.D.*	11	5	2		X_5	1	X_2		1	X_3	1	1
26	M.V.D.	10				6	5	2	2	2			
14	M.V.D.	10						+	+	+	+	+	
28	M. & A.V.D.†	9				7			5				
1	M. & A.V.D.	8	X_5	X_5	X_5	X_5	6						
3	M.V.D.	7						3	1				
27	M.V.D.	7							6				
32	M. & A.V.D.	6						7					
19	M.V.D., & I.A.D.‡	5	5										
5	M. & A.V.D.	5	8			4							
4	M.V.D.	5	3	3	3	X_3	6						
34	M. & A.V.D.	5	6	6	4	2	A_4						
36	M.V.D.	4	1	6	A_4	A_7							
2	M.V.D.	4		1									
42	M.V.D.	4				2							

*M.V.D., Mitral valvular disease.
†M. & A.V.D., Mitral and aortic valvular disease.
‡I.A.D., Intra-atrial septal defect.
Digit under individual pregnancy number indicates month at which evidence of failure first appeared.
Those pregnancies where a blank occurs under the pregnancy number were completed without complication of congestive failure.
A, abortion with subscript indicating month when failure developed; X, abortions uncomplicated by failure with subscript indicating month when pregnancy terminated.
+, Information inadequate to date onset of failure.

The effect of increasing parity upon the incidence of congestive heart failure is shown in Table IV. There was no progressive increase in the incidence of failure as the number of pregnancies increased. It can be seen that the incidence of failure during the fourth pregnancy was 11.3 per cent, exactly the same as during the initial pregnancy; it was practically the same for the fifth and sixth pregnancies. There were seven women in whom failure developed during one or more of the first three pregnancies. Only one of these patients had more than five pregnancies. The presence of this small group in the larger series accounts, in part, for the relatively constant incidence of failure in the first four pregnancies. It should be added that all of the patients in this small group were under the age of 25 years when the pregnancies complicated by cardiac decompensation

occurred, so that the deleterious effect of aging is largely excluded. There were eight patients who developed congestive failure for the first time during or after the fourth pregnancy. All of these women were over the age of 25 years and one-half of them were older than 30 years. It is our impression that the increasing age of the patient and the greater duration of the rheumatic state were factors of greater importance in the production of heart failure in these women than was the increasing parity. It is our belief that, in general, parity per se bears little relationship to the development of heart failure. This is in accord with the opinion expressed by Hamilton and Thomson[7] who stated: "We do not believe there is any special number of pregnancies when the risk for another changes."

TABLE IV. CORRELATION OF INCREASING PARITY WITH INCIDENCE OF HEART FAILURE

Para	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Total patients	53	53	53	53	39	31	27	22	13	10	4	2	1	1	1	1
Number with failure	6	5	3	6	5	4	5	3	1	2	1	0	0	0	0	0
Per cent with failure	11.3	9.4	5.7	11.3	12.8	13.0	18.5	13.6	7.7	20	25	0	0	0	0	0

In the patient with cardiac disease, the age at which she undertakes pregnancy is apparently one of the most significant factors which determine whether congestive heart failure will occur. This point has been emphasized by Hamilton and Thomson,[7] and by Bunim and Rubicius.[4] The experience in our specially selected group of women who had four or more pregnancies was very similar (see Fig. 1). There were 111 pregnancies which occurred in women between the ages of 15 and 25 years; the incidence of congestive failure was 10.8 per cent (twelve patients). In women between the ages of 26 and 35 years there were eighty-seven pregnancies with cardiac failure in 20.7 per cent (eighteen patients). Thirty-one pregnancies occurred in women between the ages of 36 and 45 years with failure developing in 35.5 per cent of them (eleven patients). In Fig. 1 the figures reported by Hamilton and Thomson[7] are also shown. The abrupt increase in the incidence of heart failure when pregnancy occurs after the age of 30 years in a patient with heart disease is clearly seen. This chart is made up from the experience of thirty-nine of our fifty-three patients and represents 229 pregnancies. In the remaining fourteen women and 135 pregnancies, the age at the time of pregnancy could not be determined with sufficient accuracy for inclusion here.

A major factor in the increasing frequency of cardiac failure in pregnancy with advancing age in the patient appears to be the greater duration of the rheumatic state which underlies the heart disease. It was possible to relate the date of onset of the initial attack of rheumatic fever to the date of confinement in 159 of the total of 364 pregnancies studied (Table V). Forty pregnancies occurred within nine years after the initial bout of rheumatic fever; there were only two instances (5 per cent) of congestive heart failure in this group. Seventy-seven pregnancies occurred ten to nineteen years after the onset of the rheumatic state; congestive heart failure occurred in fifteen (19.3 per cent) of these preg-

nancies. There were thirty-six pregnancies which occurred twenty to twenty-nine years after the first attack of rheumatic fever; cardiac failure developed in fourteen (38.8 per cent) of these. Of the six pregnancies which occurred thirty or more years after the onset of the rheumatic state, heart failure appeared in five (83.3 per cent). It is evident from this analysis that patients with long-standing rheumatic involvement have a much greater likelihood of developing congestive heart failure during pregnancy. This evidence supports the recommenda-

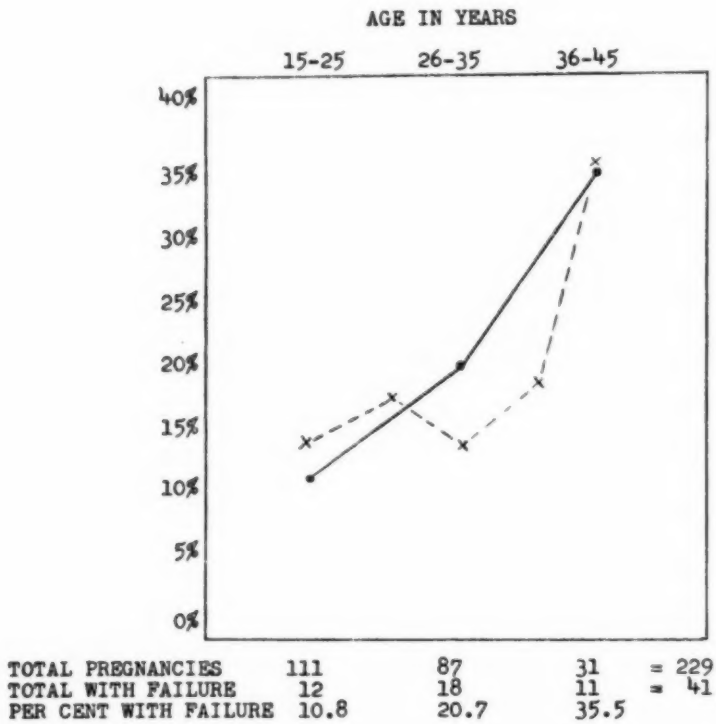

Fig. 1.—Chart showing correlation between incidence of congestive heart failure and age at which pregnancy is undertaken in multiple pregnancies in patients with rheumatic or congenital heart disease. Hamilton and Thomson - - - . Correll and Rosenbaum—.

tion of Levine[11] that, in general, women with rheumatic heart disease who desire children should marry early and have their pregnancies as soon as possible thereafter while they are still relatively young and their rheumatic state has been of relatively short duration. Furthermore, this evidence is compatible with the observations of Bunim and Rubicius[4] which indicate the value of determining the position of the patient in the natural history of her rheumatic state in order to determine the risk of pregnancy. A patient whose rheumatic state is of long duration is also usually farther along in the natural history of that disorder and is consequently a poorer risk. On the other hand, a rheumatic state of brief duration imposes the hazard of recurrence of rheumatic activity during pregnancy.

TABLE V. DURATION OF RHEUMATIC STATE AND INCIDENCE OF HEART FAILURE DURING PREGNANCY

DURATION OF RHEUMATIC STATE (YEARS)	PREGNANCIES (NUMBER)	PREGNANCIES WITH FAILURE (NUMBER)	PREGNANCIES WITH FAILURE (PER CENT)
0–9	40	2	5
10–19	77	15	19.3
20–29	36	14	38.8
30+	6	5	83.3

It seemed pertinent to determine whether or not any correlation could be found between the character and severity of the attacks of rheumatic fever and the subsequent occurrence of congestive failure during pregnancy (Fig. 2). If any such correlation does exist, it may be of practical importance in guiding the physician in his evaluation of patients who present themselves to him, since he can always elicit a detailed history regarding the earlier rheumatic manifestations. There were fourteen patients from whom no definite history of rheumatic fever could be obtained; cardiac failure occurred in only two of them (14.3 per cent). There were fifteen women who had a single acute attack of rheumatic involvement; congestive failure developed in three of them during pregnancy (20.0 per cent). A history of two attacks of rheumatic fever was obtained from sixteen patients; the heart failed during pregnancy in six women of this group (36.5 per cent). There were four women who had four attacks of acute rheumatic fever; congestive heart failure complicated pregnancy in two of them (50.0 per cent). Congestive failure occurred in two of the three women (66.6 per cent) who had seven or more attacks of rheumatic fever. Although the entire group is relatively small, these data suggest strongly that the greater the number of rheumatic recurrences, the higher the incidence of cardiac failure during pregnancy. It is probable that each recurrence damaged the heart more and more but the information available to us does not permit this conclusion. The likelihood of permanent, residual valvular damage increases with each recurrence but serious damage may follow a single, mild attack and the heart may escape serious injury despite repeated bouts of rheumatic fever. The information available to us regarding the exact nature and severity of the actual episodes of rheumatic fever was not suitable for any analysis of the relation of these factors to the course of subsequent pregnancies; it is possible that such information may prove of considerable value in dealing with this problem.

Auricular fibrillation was discovered during pregnancy in two patients (3.7 per cent) of our series. One patient (Patient 36, Table III) had auricular fibrillation and congestive heart failure during each of her four pregnancies, although the last two terminated unsuccessfully. The second patient (Patient 34, Table III) had congestive failure during each of her five pregnancies and auricular fibrillation in at least the last two of them. The incidence of auricular fibrillation in our entire group is low, especially in view of that fact that of the 229 pregnancies, in which the age at pregnancy was known, sixty-six occurred in women older than 30 years, when this arrhythmia begins to complicate rheumatic heart

disease with much greater frequency. This low incidence of auricular fibrillation may have been an important factor in the ability of these women to tolerate multiple pregnancies. The low incidence of auricular fibrillation also suggests that these patients were in a fairly early stage ("phase 3"[4]) of the natural course of their rheumatic heart disease, a stage in which the added burden of pregnancy was relatively easy for the damaged heart to bear. This is suggested also by the fact that although only two of the fifty-three patients had auricular fibrillation during their pregnancies, eight of the nineteen still living and twenty-one of the

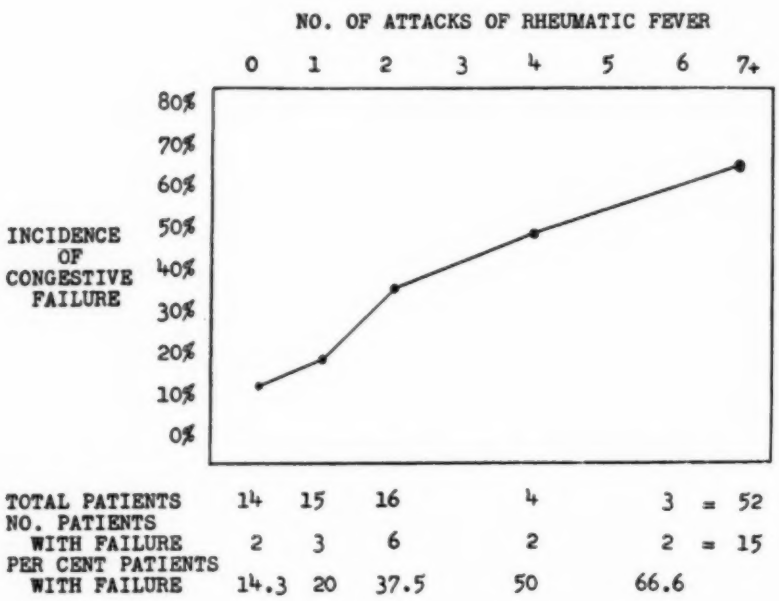

Fig. 2.—Incidence of congestive failure during pregnancy related to number of attacks of rheumatic fever.

thirty-four women who have died eventually developed auricular fibrillation. It is of further interest that of the thirteen patients who died without first developing auricular fibrillation, nine died of noncardiac disorders or acute endocarditis or septicemia.

We have been unable to correlate the onset of auricular fibrillation with the time of death thereafter because information regarding the exact time of onset of the arrhythmia was rarely available. It is our impression that the appearance of auricular fibrillation has a more serious prognosis so far as length of life is concerned than does the development of congestive heart failure in the absence of this arrhythmia. Auricular fibrillation appearing during pregnancy is probably more clearly a sign of an advanced stage of rheumatic heart disease than is the occurrence of congestive failure during the stress of childbearing. DeGraff and Lingg[12] have reported that in all adults with rheumatic heart disease the mean duration of life after the onset of auricular fibrillation is only two years. They found that after the arrhythmia appeared 34.3 per cent died within one year

and approximately 70 per cent died within two years. Stroud, Laplace, and Reisinger[13] reported the duration of life after auricular fibrillation to be two and one-half to three years. It is of considerable interest that in the experience of Hamilton and Thomson[7] the expected maternal mortality in pregnant cardiac patients with auricular fibrillation is 34 per cent, a figure which closely resembles the first-year mortality of DeGraff and Lingg. The similarity of these two figures raises the question whether auricular fibrillation really does increase the risk of pregnancy in the patient with heart disease if the arrhythmia in a nonpregnant patient carries a one-year mortality of 34.3 per cent. It must also be pointed out, in this connection, that Hamilton and Thomson[7] reported an anticipated annual mortality rate of only 8 per cent in nonpregnant cardiac women with auricular fibrillation during the childbearing age.

No definite correlation could be demonstrated between the type of valvular disease and the development of congestive heart failure during pregnancy in the examples encountered in this special group of cases. Cardiac failure was as common in those women with mitral valvular disease alone as in those with both mitral and aortic valvular disease. It is possibly of some significance that no patient with aortic valvular disease alone was encountered in this series. At least a few such patients would be found in almost any general unselected series of patients with rheumatic heart disease. This study was confined to women with four or more pregnancies; this criterion may have automatically eliminated patients with aortic valvular disease, if that lesion is incompatible with multiple pregnancies. Hamilton and Thomson[7] have expressed the belief that patients with free aortic regurgitation are subject to sudden untoward developments during pregnancy and must be observed with even more than usual care. Another observer has expressed the opinion that "free" aortic regurgitation is a contraindication to pregnancy.[14] The experience of one of us (F. F. R.) with isolated patients has been in accord with these opinions. On the other hand, some workers feel that lesions of the aortic valve are of no more serious significance than lesions of the mitral valve and do not increase the gravity of the immediate prognosis in pregnancy.[13] The patient with congenital cardiovascular disease involving the pulmonary arterial system tolerated ten pregnancies remarkably well and with no sign of failure. Her tolerance was not unlike that of patients with interauricular septal defects.[16]

So that we might study the incidence of congestive failure in these patients from another point of view, they were divided at each pregnancy into favorable and unfavorable categories according to the criteria and classification of Hamilton and Thomson[7] (Table VI). There were 314 pregnancies in patients in the favorable category; congestive failure occurred in only fifteen (4.7 per cent) of these pregnancies. Of the fifty pregnancies occurring in patients in the unfavorable category, there were twenty-six (52 per cent) instances of heart failure. The striking difference between these two groups indicates the usefulness of this type of classification in advising cardiac patients regarding the possibility of heart failure during pregnancy and in guiding the physician who is managing these patients during pregnancy.

TABLE VI. HEART FAILURE IN FAVORABLE AND UNFAVORABLE CARDIAC PATIENTS

CLASSIFICATION DURING PREGNANCY	PATIENTS (NUMBER)	HEART FAILURE (NUMBER)	PER CENT
Favorable	314	15	4.8
Unfavorable	50	26	52.0

TYPE OF DELIVERY

Of the 364 pregnancies, 328 deliveries were by the vaginal route. There were only three cesarean sections all of which were performed for obstetric indications. There were two therapeutic abortions and thirty other abortions which were spontaneous or criminally induced. There was one surgical removal for a ruptured ectopic pregnancy. The deliveries were performed by a large number of obstetricians and the predominance of vaginal deliveries is not the result of a predetermined departmental policy. The small number of operative deliveries was a surprising fact when we first became aware of it. It is apparent that this group of fifty-three women with heart disease were able to tolerate multiple vaginal deliveries even though some of them had congestive failure. This experience emphasizes the developing viewpoint that in pregnant cardiac patients cesarean section should be performed primarily because of obstetric indications.

SUBSEQUENT COURSE OF CARDIAC PATIENTS SURVIVING MULTIPLE PREGNANCIES

At the present time the character of the subsequent course of multiparous patients with heart disease has not been clearly defined. The duration of life after the childbearing period, the subsequent incidence of heart failure, and the nature of this decompensation are features which have attracted only moderate interest. Reid,[9] Boyer and Nadas,[10] and others were unable to demonstrate any shortening of the life span in multiparous women with heart disease as compared to nulliparous cardiac patients. These studies cannot be said to exclude all possibility of deleterious effects of pregnancy upon the diseased heart because in most of these studies the factors of duration and severity of the underlying rheumatic process were not controlled, and the duration and character of the terminal illnesses were not compared. Finally the nulliparous groups may well have included many cardiac invalids who died early before reaching a marriageable age or who avoided marriage because of their heart disease. The likelihood is that such patients would die at an early age, thereby reducing the average age level of nulliparous cardiac patients. Any comparison of multiparous and nulliparous cardiac patients must take a large number of factors into account and must include large numbers of patients who are comparable in all respects except as regards pregnancy. Until such studies are reported it is not possible to evaluate completely the ultimate effect of pregnancy upon the diseased heart.

The relationship of congestive heart failure during pregnancy to its appearance during later life was studied by reviewing the course of the fifty-three patients (Table VII). There were fifteen patients who had congestive failure

during pregnancy. Nine of these women were still living and failure had appeared in five of them (55.5 per cent). Five of the remaining six who had died developed decompensation before death (83.3 per cent). There were thirty-eight women who did not have failure in any of their pregnancies. Ten of these patients were living and heart failure had appeared in five (50 per cent). Twenty-eight of this group without failure during pregnancy had died and decompensation had occurred in nineteen some time before death (67.7 per cent). Although this group is relatively small, these results suggest that ultimate cardiac failure is somewhat more likely to occur in a woman who has heart failure during pregnancy than in one who does not.

TABLE VII. RELATION OF FAILURE IN PREGNANCY TO SUBSEQUENT DEVELOPMENT OF HEART FAILURE

	NUMBER WITH FAILURE IN PREGNANCY	NUMBER WITHOUT FAILURE IN PREGNANCY	NUMBER WITH SUBSEQUENT FAILURE	PER CENT
Living	9		5	55.5
Dead	6		5	83.3
Living		10	5	50.0
Dead		28	19	67.8

In Table VIII, an attempt is made to correlate the ultimate life span with the presence or absence of congestive failure during multiple pregnancies. There were thirty-four women who were followed up to the time of death. Six of this group had congestive failure during pregnancy and their mean age at death was 44.0 years. Twenty-eight of these patients had multiple pregnancies without failure and their average age at death was 55.0 years, their life being nearly eleven years longer than that of those who had congestive failure. There were nineteen patients who were living at the time of this study. Nine of them developed cardiac decompensation during pregnancy and their mean age is now 41.4 years. There are ten who did not have failure during pregnancy and their mean age is now 49.0 years. These observations suggest that the ultimate life expectancy is appreciably longer in those women who do not have failure during pregnancy. Furthermore, since the average ultimate age of all those known dead was 49.5 years, it may also be stated that multiple pregnancies are not incompatible with a fairly long life span in many women with significant valvular heart disease.

TABLE VIII. RELATION OF CONGESTIVE FAILURE DURING PREGNANCY TO SUBSEQUENT LIFE EXPECTANCY

	LIVING		DEAD	
	NUMBER	AVERAGE AGE	NUMBER	AVERAGE AGE AT DEATH
Failure during pregnancy	9	41.4 years	6	44.0 years
No failure during four or more pregnancies	10	49.0 years	28	55.0 years

An effort was made to relate the duration and nature of the ultimate cardiac decompensation to the course of the multiple pregnancies. Although the group was small and details of the final illnesses were often unavailable, it was our impression that the degree of valvular damage present and particularly the cardiac arrhythmias which developed in later life were more important factors in determining the nature of the final illness than was the presence or absence of congestive failure during pregnancy.

SUMMARY

A group of fifty-three cardiac patients who had four or more pregnancies have been studied. All of these women had rheumatic heart disease with the exception of one patient who had idiopathic pulmonary arterial dilatation. These patients had a total of 364 pregnancies or nearly seven pregnancies per patient.

The maternal mortality was only 1.3 per pregnancy and only one of the five deaths was related to congestive heart failure. Congestive heart failure occurred in fifteen of the fifty-three patients or in forty-one of the 364 pregnancies (11.3 per cent), an incidence less than that usually reported in cardiac patients. Our findings suggest that these women were able to tolerate the burden of pregnancy better than the average cardiac woman in the childbearing period. Congestive heart failure did not increase in frequency as the number of pregnancies increased, a finding which confirms the belief that parity per se bears no direct relationship to the development of heart failure.

The age of the patient, the duration of the rheumatic state, and the number of attacks of rheumatic fever all seem more important factors influencing the course of the pregnancy in the cardiac patient than the actual number of pregnancies she has borne previously.

Auricular fibrillation was uncommon in this special group of patients with multiple pregnancies, a fact suggesting they were in a relatively early stage of the natural history of their rheumatic heart disease. Congestive failure occurred much more commonly in the unfavorable (52 per cent) than in the favorable (4.7 per cent) group.

In all of the pregnancies which came to full term delivery was accomplished by the vaginal route with the exception of three cesarean sections performed for obstetric reasons. This confirms the belief that in cardiac patients operative delivery should be performed primarily for obstetric indications.

The ultimate life span was greater and the incidence of subsequent congestive failure was less in those women who were able to tolerate multiple pregnancies without developing cardiac decompensation than in those who had heart failure. This series of patients indicates that multiple pregnancies are compatible with a considerable life expectancy in some women with heart disease. It is emphasized, however, that in considering the problems of pregnancy every patient with heart disease must be evaluated individually in the light of many factors including her age, the duration of the rheumatic state, the nature of the original rheumatic disease, the cardiac reserve, and the course of earlier pregnancies.

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Clinical Reports

NONPENETRATING CHEST INJURY AND POSTERIOR MYOCARDIAL INFARCTION PATTERN

Report of Two Cases

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THE possible causal relation of nonpenetrating thoracic trauma and subsequent evidence of myocardial injury presents a problem of considerable medicolegal importance.[1] The physician who is requested to provide medical testimony in cases involving workmens' compensation and insurance claims is faced with three paths of reasoning: (1) The blow and the myocardial disturbance are unrelated; the myocardial findings occurred in the natural course of events. (2) The trauma aggravated established coronary artery disease. (3) The externally applied force is sufficient to definitely injure an otherwise normal myocardium. Some skepticism has been expressed as to whether the last alternative occurs. In *Modern Concepts of Cardiovascular Disease*, in 1942, Crawford[2] stated: "One might also state damage to the normal heart by trauma is uncommon and that, excluding penetrating wounds, no severe, permanent damage to the normal heart takes place except in rare instances." Stroud,[3] in 1940, expressed a similar opinion.

The writer has recently seen two examples of nonpenetrating trauma to the anterior wall of the chest in relatively young (aged 29 and 34 years) men which were immediately followed by clinical and electrocardiographic evidence of posterior myocardial injury.

CASE REPORTS

Case 1.—The patient was a 34-year-old white man. At 2 A.M. on December 19, he lost control of his automobile which struck a tree. He did not lose consciousness, but suffered a severe blow on the anterior portion of his chest from being thrown against the steering wheel. His pelvis was fractured, and he sustained multiple superficial cuts.

When examined, approximately two hours after the accident, the anterior wall of the chest was very tender. A gallop rhythm was heard. The blood pressure was 100/60 and the pulse rate 105 beats per minute. The blood sugar reading was 94 mg. per 100 c.c. and blood cholesterol 190 mg. per 100 cubic centimeters. An electrocardiogram (Fig. 1), made approximately seven hours after the accident revealed deep Q waves and elevated RS-T segments in Leads II and III

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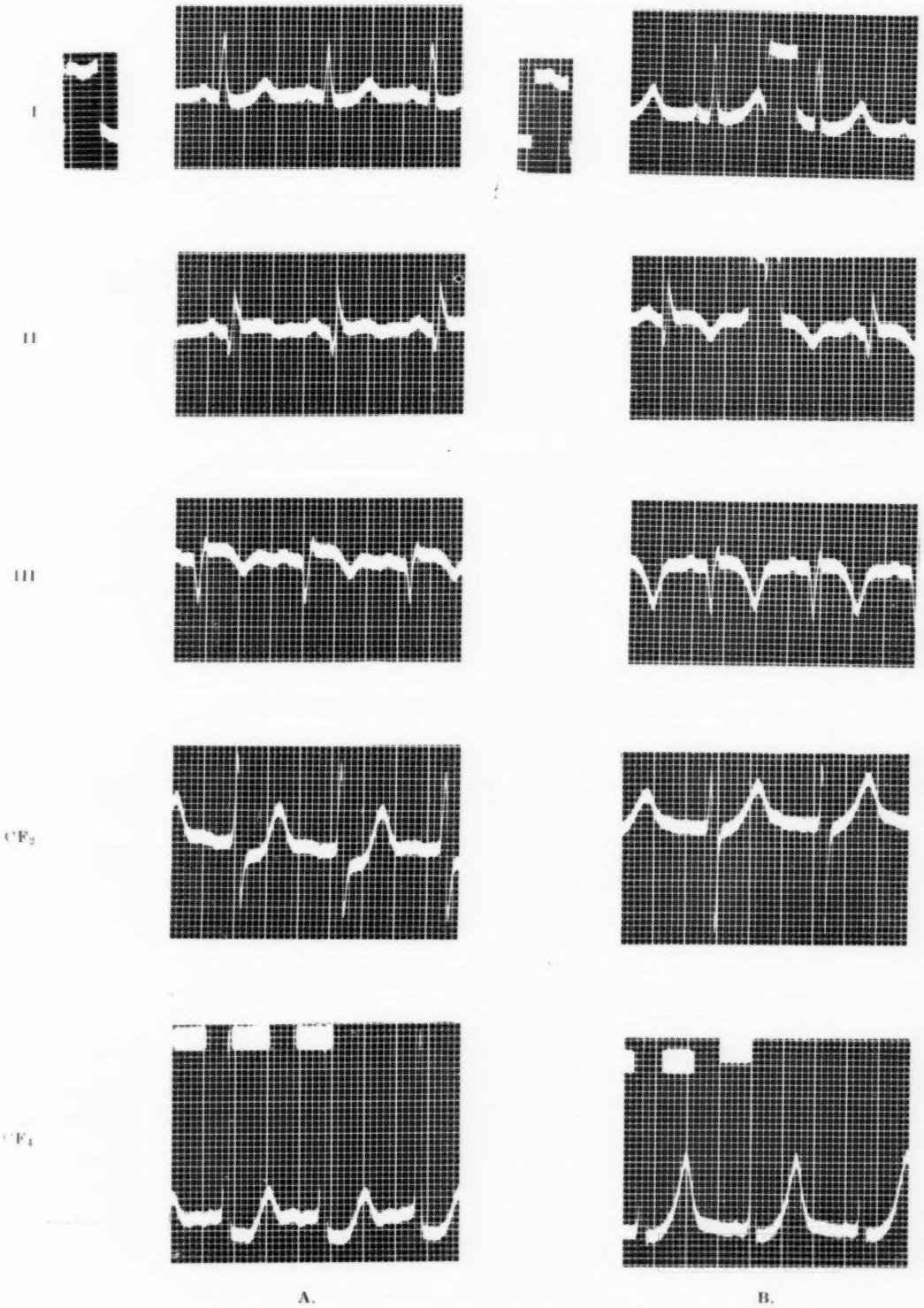

Fig. 1.—*A*, Electrocardiograms made December 19, seven hours after accident. *B*, Tracings made January 26, five weeks after accident.

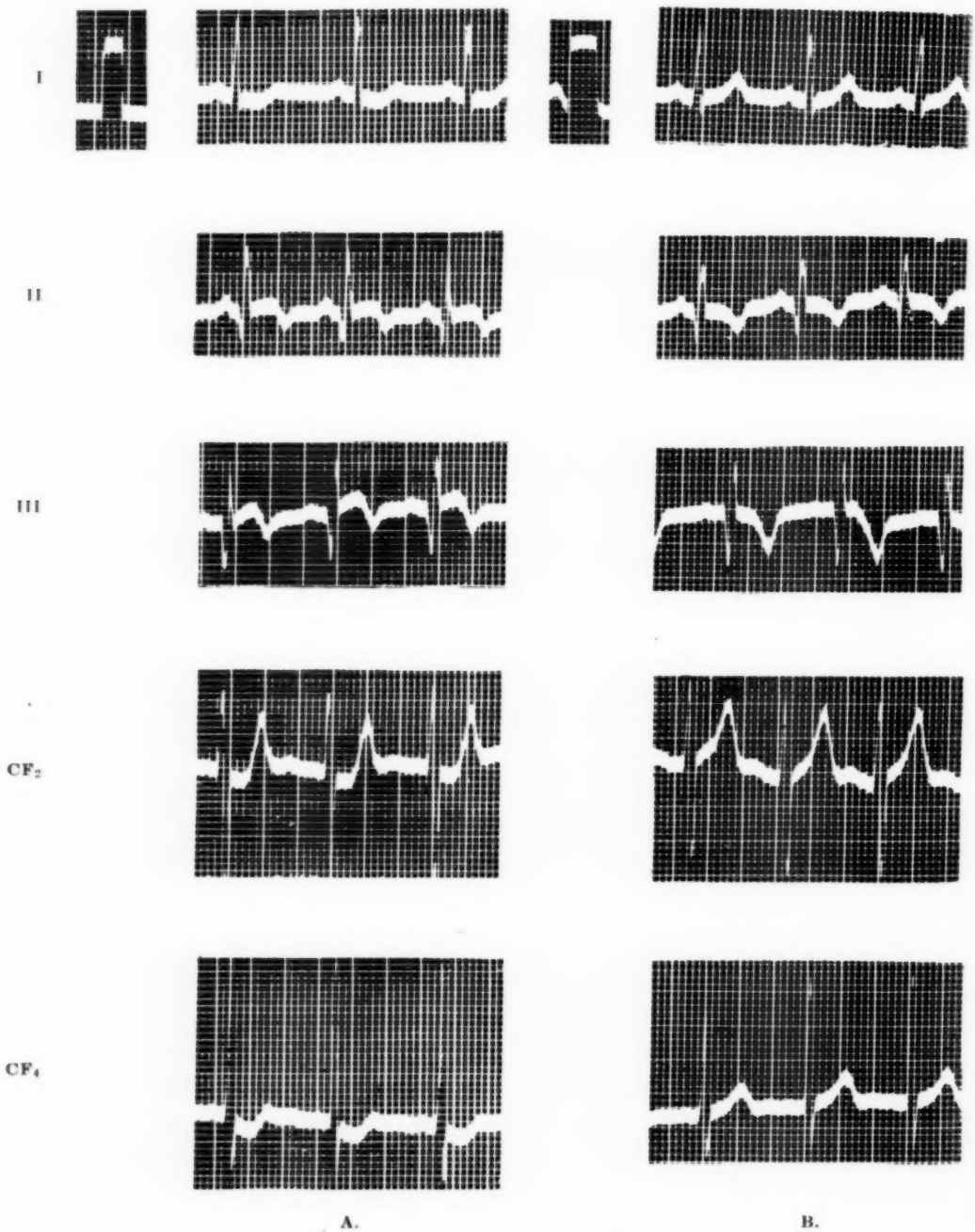

Fig. 2.—*A*, Electrocardiograms made February 19, twenty-one hours after injury. *B*, Tracings made March 20, one month after injury.

with depressed RS-T segments in Lead I and in the chest leads. Subsequent daily records followed the evolution which was considered typical of a posterior myocardial infarction. A tracing obtained one month after the injury (Fig. 1) recorded deep Q waves and coved, inverted T waves in Leads II and III and peaked, upright T waves in Lead I and in the chest leads.

The gallop rhythm disappeared in a matter of hours following the accident. Healing of the various injuries took place without incident and the patient became ambulant without developing angina or decompensation.

The patient's past history revealed that he was a service man on furlough. He had recently been examined and told that his blood pressure was normal. He denied any history of angina, dyspnea, or orthopnea.

CASE 2.—The patient was a 29-year-old man employed as a stevedore. During the afternoon of February 18, while working, he was struck squarely in the anterior midportion of the chest by a crate weighing 75 pounds. He staggered, but was not knocked to the ground. After regaining his "breath" he continued to work. He soon noticed a heavy ache in the midchest which could be relieved only by resting. He left his work, returned to his room, and rested overnight. He did not perspire during this time. Upon arising on February 19, he felt well, but while dressing the "ache" returned and was accompanied by shortness of breath. Minimal effort brought on the discomfort and dyspnea. He came to the clinic at 11 A.M. on February 19.

The patient had no past history of angina or other significant cardiac complaints. He had served as an enlisted man during the war and had been discharged eight months prior to admission. His blood pressure had never been known to be elevated.

An electrocardiogram (Fig. 2) was obtained approximately twenty-one hours after the injury. There were deep Q waves and elevated RS-T segments in Leads II and III with depressed RS-T segments in Lead I and the chest leads.

Physical examination revealed no abnormality other than a bruised and tender area over the sternum. The blood pressure was 95/65. The blood sugar reading was 105 mg. per 100 c.c. and the blood cholesterol 200 mg. per 100 cubic centimeters.

Following admission to the hospital the patient was promptly placed in bed. The course of illness was uneventful. Serial electrocardiograms were compatible with a diagnosis of myocardial injury. He was last seen three months after the accident and was ambulant, but having slight angina.

COMMENT

These findings may have been coincidental and not related to the accidents. It would seem, however, that the sudden development, in young (34 and 29 years of age), normotensive, nondiabetic men, of clinical and laboratory evidence of posterior myocardial infarctions immediately following severe trauma to the anterior wall of the chest is strong evidence that the relationship was more than casual.

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QUINIDINE ALLERGY

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ALTHOUGH allergic reactions to quinine have been described repeatedly, relatively little consideration appears to have been accorded the possibility of a similar response to quinidine. Emphasis has been placed rather upon the occurrence of untoward cardiac reactions, and few instances of quinidine hypersensitivity have been recorded.[1,2,3]

Nevertheless, the awareness of the possibility of an unusual reaction to quinidine is indicated by the generally practiced administration of a preliminary test dose. This precaution is intended not only to prevent the rare and serious cardiac effects, but also to determine the existence of cinchonism. It is worthy of emphasis here that an immediate allergic or anaphylactic reaction might be anticipated only after a previous exposure to quinidine or to a related drug such as its optical isomer, quinine. On the other hand, in those individuals who have not received quinidine previously, allergy to the drug, as in other drug and serum reactions, will become evident clinically only after an incubation period, usually of five to ten days or more. The observation of two instances of hypersensitivity to quinidine sulfate has prompted this report. The first patient exhibited thrombocytopenic purpura and a severe febrile reaction to the drug and offered a considerable problem in diagnosis. The advanced age of this patient, in addition, emphasizes the fact that allergy, particularly of the acquired type, may occur in later years. In Case 2 a febrile and urticarial reaction occurred.

CASE REPORTS

CASE 1.—A 76-year-old woman was admitted to the Mount Sinai Hospital, Nov. 21, 1946 (Service of Dr. I. Snapper), complaining of recurrent chills and fever of ten months' duration. She stated that she had been well until about one year prior to admission, when she had had an upper respiratory tract infection, characterized by fever to 102° F., malaise, and mild sore throat. These complaints subsided after three weeks of symptomatic treatment but she then noted attacks of tachycardia.

Two weeks after the conclusion of the initial episode she experienced a shaking chill with a temperature of 103° F., vomiting, and pain in both shoulders, arms, and upper back, associated with weakness and anorexia. These symptoms persisted for two days. There were three additional attacks of similar nature. The last occurred six weeks before admission to the hospital and was also characterized by the presence of a gradually fading, large, ecchymotic area over the abdomen, unassociated with any arthralgias. Three days before entry, she again developed nausea, malaise, a shaking chill, vomiting, and generalized abdominal pain, accompanied by several loose, bloody bowel movements and the appearance of purpuric areas over the abdomen.

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Physical examination revealed a well-developed, well-nourished, kyphoscoliotic, elderly woman with pale conjunctivae and mucous membranes. Innumerable petechiae of the chest, arms, and thighs, and several large ecchymoses of the arms and legs were noted. The buccal and palatal mucosae were the site of several multiple hemorrhagic foci. The lungs showed slight dullness to percussion at the left base with moist râles. The heart was slightly enlarged to the left. A soft blowing precordial systolic murmur was audible and the rhythm was regular. The blood pressure was 196/80. The liver edge was just felt, while the spleen edge was questionably palpable.

The blood hemoglobin was 78 per cent (Sahli); red blood cells numbered 3,380,000, and the white blood cells were 9,900 per c. mm. with a differential count of polymorphonuclears 72 per cent, nonsegmented forms 6 per cent, and lymphocytes 20 per cent. Only an occasional platelet was seen; the reaction to the tourniquet test was positive.

The blood coagulation time was eight minutes (Lee-White) and the bleeding time one minute. Clot retraction was fair at one hour; prothrombin index was 100 per cent. Erythrocyte sedimentation rate was 46 mm. per hour (Westergren); platelets numbered 60,000 per c. mm.; a blood culture remained sterile. Renal phenosulfonphthalein excretion was 85 per cent. X-ray examination of the chest and an electrocardigram disclosed no abnormalities. Reactions to the blood Wassermann and cephalin flocculation tests were negative; the blood urea and sugar values were within normal limits.

Bone marrow studies on November 27 revealed megakaryocytes with definite platelet formation. On December 11 the blood platelets numbered 40,000 per c. mm.; eosinophiles were not noted.

The possibility that the purpura and thrombocytopenia might have been due to drugs was now accorded serious consideration. On inquiry it was found that the patient's medication in the preceding year had consisted, among other substances, of morphine sulfate, amidopyrine, Phenacetin, acetanilide, atropine, phenobarbital, chloral hydrate, codeine sulfate, aspirin, and quinidine sulfate. Of these the last mentioned seemed the most provocative for purposes of investigation.

A trial dose of 0.2 Gm. of quinidine sulfate was given on November 30. Four hours later, the patient developed malaise, chilliness, and a temperature rise to 103.2° F., which later reached a level of 104° Fahrenheit. Many new generalized ecchymoses appeared on the following day. The blood platelets, which had been 250,000 per c. mm. before the test dose, fell to 100,000 per c. mm. three days later, and at the end of one week were found to be 50,000 per cubic millimeter. On December 11, 0.03 Gm. of quinidine sulfate was administered, succeeded by a rise in temperature to 100.8° F., but without the reappearance of the purpura. Subsequently quinine sulfate was given in doses of 0.03 and 0.12 Gm. without reaction, but when 0.6 Gm. was given, temperature to 101.8 F., developed, unaccompanied by purpura. Reaction to a scratch test with 1 per cent solution of quinidine sulfate was negative both on direct test and passive transfer. Reaction to a patch test with 5 per cent quinidine in lanolin was likewise negative. An attempt to demonstrate precipitins for quinidine in the patient's serum was unsuccessful.

These results strongly suggested that allergy to quinidine sulfate was responsible for the clinical picture, and on this basis it was now possible to reconstruct the sequence of events in the patient's past history. She had been seen by a cardiologist because of repeated episodes of palpitation of sudden onset and offset, following an upper respiratory infection. Examination at that time disclosed no evidence of organic heart disease, and capsules of quinidine sulfate, 0.2 Gm., were prescribed, to be taken three times daily after meals. The patient distinctly recalled that she had had no chills before taking the quinidine, and that she was able to take the drug for five days without any ill effect. Following this period, the first attack of chills and fever occurred. It was because of this symptom-free incubation period preceding the development of an allergic response, that the fever had not been ascribed to the quinidine.

CASE 2.—The patient was a 50-year-old, white, moderately obese woman, with essential hypertension (180/110), and chronic cholecystitis and cholelithiasis. There was no detectable cardiac enlargement. She had had recurrent paroxysms of tachycardia with a rate averaging 180 beats per minute unrelieved by carotid sinus or eyeball pressure. Accordingly, following a trial dose, she was given 0.2 Gm. of quinidine sulfate every three hours for five doses the first

day and three times on the second day. On the afternoon of the third day, she developed a generalized pruritic maculopapular eruption (involving the face and extremities), anorexia, malaise, and a temperature of 100.2° F. by mouth. In view of previous experience with reactions of this type, following administration of quinine sulfate, a quinidine reaction was suspected and the drug, therefore, discontinued. Within two days there was complete subsidence of the skin eruption and temperature elevation. The heart rate, incidentally, had been restored to normal.

Two weeks following this episode, in order to determine whether the patient's manifestations were due to the drug, a test dose of 0.2 Gm. of quinidine was given and repeated four hours later. A maculopapular eruption reappeared over the patient's neck, chest, and abdomen, and her temperature rose to 100° F. by mouth. All these manifestations again subsided within two days after discontinuance of the medication. The patient refused skin testing or any other investigation of her allergy.

DISCUSSION

Sharp rises in temperature due to drug allergy have been observed frequently. In recent years the drugs most commonly responsible for such reactions have been sulfathiazole, thiouracil, and particularly nirvanol. It has been well known that febrile reactions of varying degrees may follow administration of a great variety of drugs, ranging from the barbiturates to penicillin, while thrombocytopenic purpura has been reported, especially after medication with quinine, Sedormid, the barbiturates, and arsenicals. Peshkin and Miller[4] described a case of purpura due to quinine in which the platelet count dropped to 100,000 per cubic millimeter. In this patient clot retraction was absent, and reactions of scratch and intradermal tests were positive with quinine salts in a 1 to 10 per cent solution but negative with quinidine. More recently Schrager and Kean[5] reported nine cases of purpura due to quinine, in three of which the platelets fell to less than 100,000 per cubic millimeter. However, most instances of drug purpura appear to have been thrombocytopenic in variety. The level of blood platelets may fall rapidly after exposure to a specific drug, often in less than one hour, at other times not before twenty-four hours or more have elapsed. In the first case described herein, thrombocytopenia persisted for more than a week. It is worthy of comment that fever is not an invariable accompaniment of drug purpuras, and has been absent, for example, in purpuric reactions due to Sedormid.

Despite the structural similarity of quinine and quinidine, Dawson and Garbade[6] observed that a patient might be markedly sensitive to quinine and to all the levorotatory isomers of the cinchona group of alkaloids, yet tolerate quinidine and all the dextrorotatory alkaloids. In this connection, Sanders[7] reported an instance of intense quinine sensitivity which precluded the further use of the drug for the patient's malaria. A positive reaction to the scratch test to quinine was demonstrated; the reaction with quinidine was negative, and treatment with the latter proved both successful and uneventful. Dawson, Sanders, and Tomlinson,[8] however, found that, while some quinine-sensitive persons could tolerate quinidine and other dextrorotatory alkaloids, this was not invariably the case. The first patient herein reported illustrates that sensitivity may exist to both quinine and quinidine.

Although reactions to skin tests are typically negative in drug allergy, quinine is an exception and may give a positive reaction with the scratch method in sen-

sitive subjects.[6] The reaction may be negative, however, even in the presence of exquisite clinical sensitivity, as in our first patient in whom reaction to the quinidine scratch test was negative.

The treatment of patients in whom a quinidine effect is desired, and where sensitivity to the drug has been manifested may offer considerable difficulty. In such instances one may be able to resort to quinine, especially when reaction to the scratch test is positive to quinidine and negative to the former. Even here, however, quinine should be administered with caution. In extreme instances, because of the existence of multiple drug sensitivities, oral desensitization with quinidine sulfate might be considered—a method which has been carried out with some success with quinine.[10] Finally, in patients exhibiting auricular fibrillation or nodal tachycardia, for whom, because of allergy, both drugs are contraindicated, Atabrine might be tried.[11]

SUMMARY

Two instances of allergy to quinidine sulfate are described. The first patient manifested repeated episodes of chills and fever to 104° F., associated with thrombocytopenic purpura. These were proved to be due to quinidine allergy by the reproduction of the clinical picture and thrombocytopenia following a single oral dose of 0.2 Gm. of quinidine sulfate. Reaction to the scratch test with quinidine was negative. A febrile reaction without purpura likewise followed the oral administration of 0.6 Gm. of quinine sulfate. The second patient's reaction was characterized by low-grade fever and a pruritic maculopapular eruption induced by quinidine sulfate on two occasions. Allergy to the cinchona alkaloids is briefly reviewed and the practical management of quinidine allergy discussed.

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CONGENITAL COARCTATION OF THE ABDOMINAL AORTA A THEORETICALLY REVERSIBLE TYPE OF CARDIAC DISEASE

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THE presence of cardiac enlargement or congestive heart failure in a child may present a difficult problem in differential diagnosis. One of the rare conditions which may cause heart failure in a child is congenital coarctation of the abdominal aorta. This unusual anomaly may be identified relatively easily if it is kept clearly in mind as a possibility in all children who suffer from heart failure. Early diagnosis is especially important because of the possibility of surgical correction of the condition. During the past 115 years this abnormality has been described in the records of autopsies performed upon eight patients.[1-8] In few of these instances was an accurate ante-mortem diagnosis established. Coarctation of the abdominal aorta has been considered congenital in patients previously reported because of the absence of histologic changes characteristic of acquired disease. In these patients the association of other congenital vascular defects was required to corroborate the diagnosis. The present report consists of the record of a patient who had congenital coarctation of the abdominal aorta and a congenital anomaly of the vessels arising from the aortic arch. The purpose of this presentation is to describe ante-mortem and post-mortem findings in this patient, to point out the features which aid in diagnosis, and to emphasize the possible surgical reversibility of this condition.

CASE REPORT

A 12-year-old Japanese girl entered the hospital on Nov. 2, 1946, complaining of lassitude and weakness of three years' duration. No history of cyanosis or other symptoms referable to the cardiovascular system was elicited. Examination disclosed an underdeveloped girl. The right radial and both femoral pulses were not palpable and the blood pressure was difficult to measure by auscultation. A systolic pressure of 40 mm. of mercury was found in the left brachial artery, using the palpatory method. The seventh to twelfth intercostal arteries were palpated bilaterally and were found to pulsate with the heart beat. The left border of the heart was enlarged. A Grade 2 systolic murmur was heard in the pulmonary area. A Grade 1 systolic murmur was heard posteriorly in the interscapular region. Auscultation along the spinal column posteriorly revealed a systolic murmur of maximum intensity in the upper lumbar region. Auscultation of the abdomen in the region of the umbilicus revealed a Grade 2 systolic murmur of maximum intensity in the periumbilical region. Anteriorly, the murmur could be heard as low as the pubis and as high as

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the xiphoid process, decreasing in intensity as the stethoscope was moved away from the umbilicus. No thrill could be detected over this region. A thrill and a coarse systolic murmur were found in the right supraclavicular fossa. No ankle edema or other signs of right ventricular congestive heart failure were found. Roentgenograms of the chest demonstrated enlargement of the left ventricle (Fig. 1). Evidence of chronic passive congestion of the lungs was present, as indicated

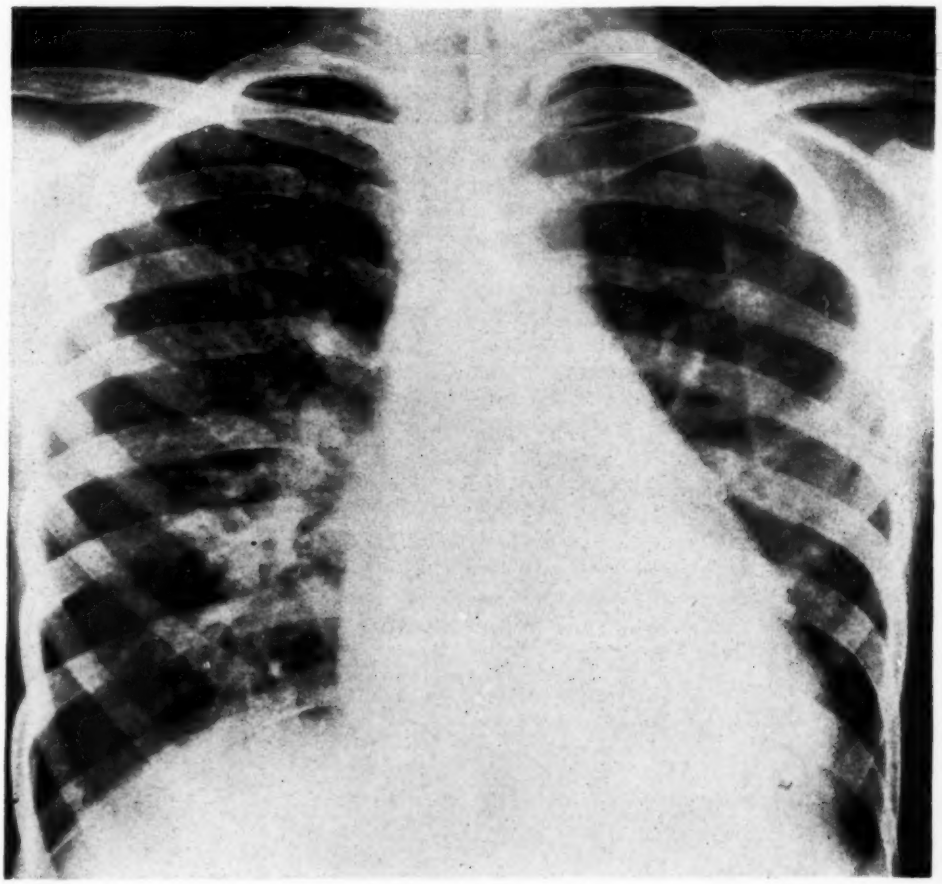

Fig. 1.—Roentgenogram of the chest during first admission shows left ventricle enlargement with chronic passive congestion of the lungs. No pathologic notching of the ribs is present.

by the increased density of shadows in the proximal third of the lung fields. Typical notching of the ribs was absent. An electrocardiogram (Fig. 2,*A*) revealed right axis deviation of the QRS complex with a transient 2:1 auriculoventricular heart block. The patient was given antibiotics and digitalis and was discharged from the hospital.

On Nov. 18, 1946, she re-entered the hospital because of edema of the ankles. Physical examination at that time revealed the presence of advanced right and left ventricular congestive heart failure. Peripheral edema extended to the level of the scapulae and was present to a lesser degree in the upper extremities. Subcrepitant râles were heard over the lung fields bilaterally. Roentgenograms demonstrated an increase in cardiac size, extensive pulmonary congestion, and right pleural effusion. Pathologic notching of the rib margins was absent. An episode of second-degree A-V heart block of the Wenckebach type was recorded (Fig. 2,*B*): this lasted twelve hours.

The Decholin arm-to-tongue circulation time was thirty-one seconds. The patient failed to respond to digitalis, mercurial diuretics, thiamine chloride, and a low-sodium diet. She expired during an attack of acute pulmonary edema on Dec. 12, 1946.

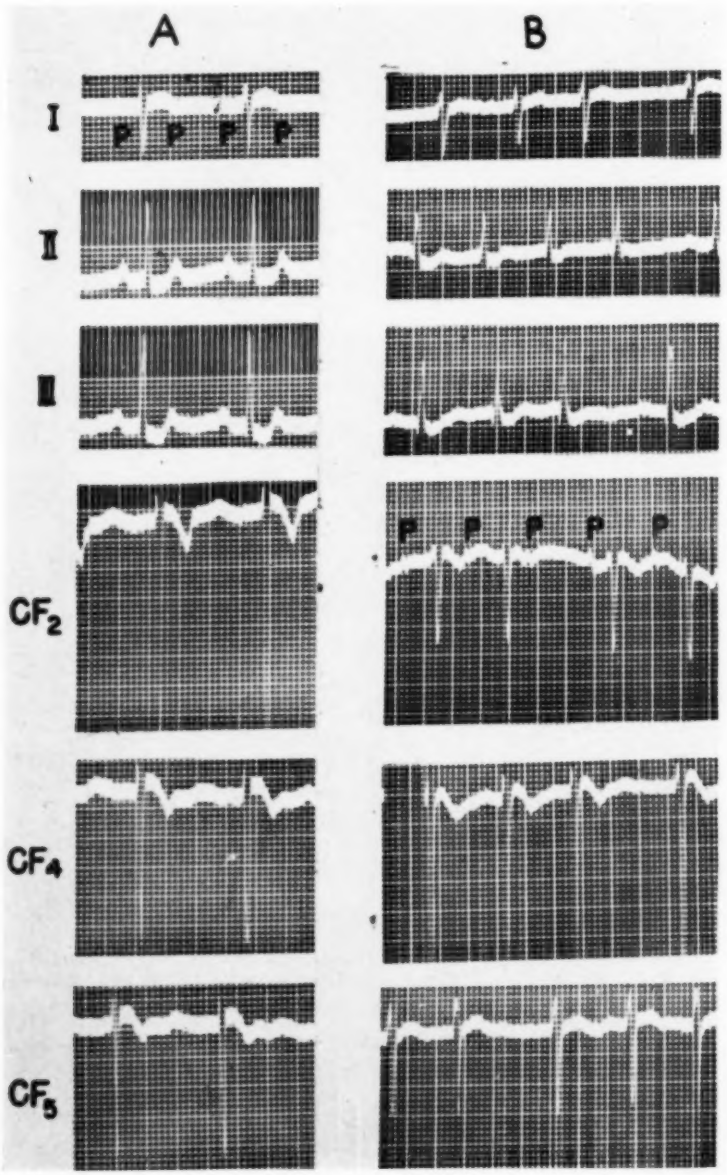

Fig. 2.—*a*, Electrocardiogram made during first admission. This shows right axis deviation of the QRS complexes with a transient 2:1 A-V heart block. *B*, Electrocardiogram made during the second admission. This shows record degree A-V block of the Wenckebach type.

Autopsy.—

Gross Examination: The body was that of an underdeveloped 12-year-old girl. Edema of the body and lower extremities was present. The heart was enlarged and the ventricles were greatly dilated. The left ventricle was hypertrophied. The valves, endocardium, and coronary

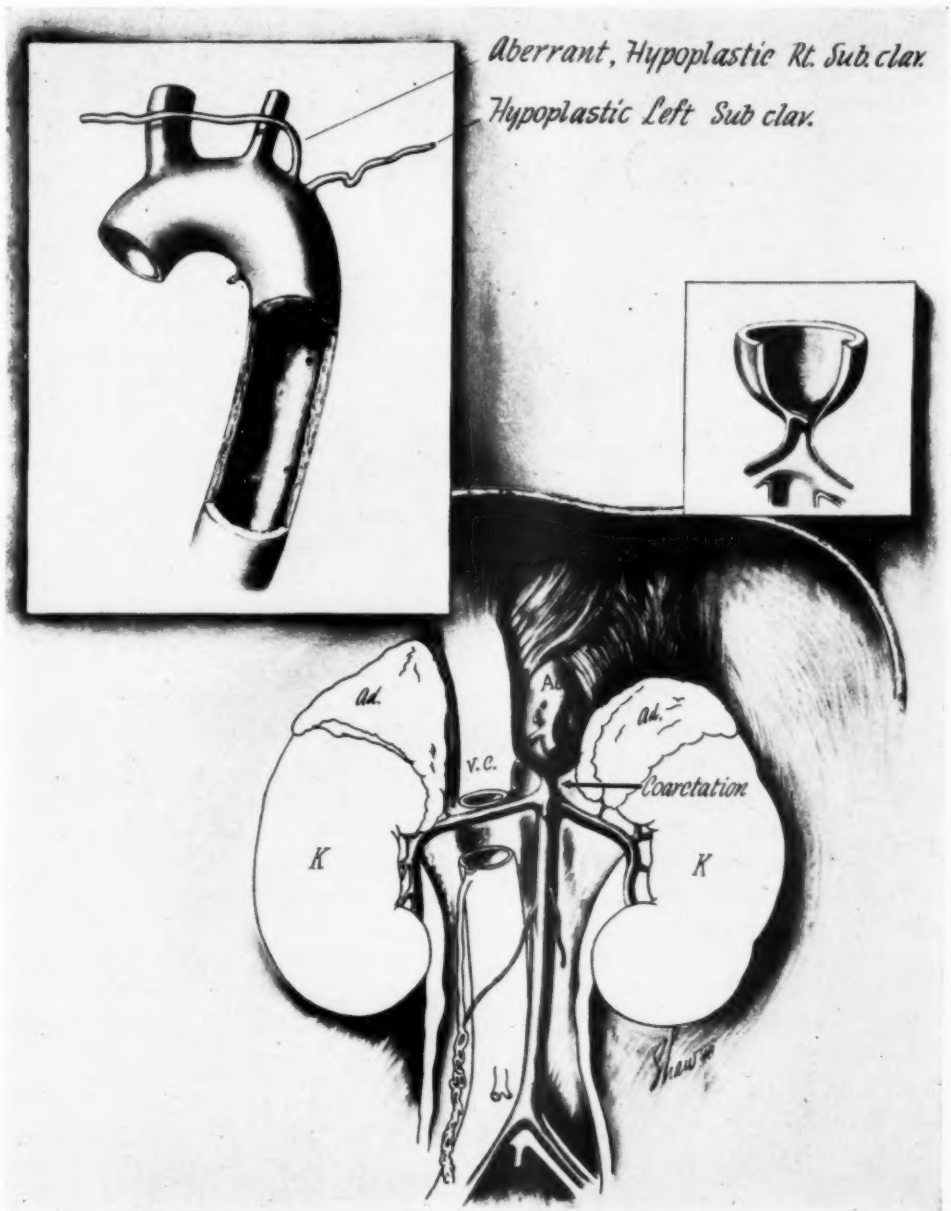

Fig. 3.—Autopsy findings illustrating anomalous origin of right subclavian artery from aortic arch, hypoplasia of right and left subclavian arteries, and abdominal coarctation above the renal arteries.

ostia were normal. The ductus arteriosus and foramen ovale were closed. The aortic arch (Fig. 3) was dilated. The following vessels were identified as branches of the aorta: a large right common carotid, a normal-appearing left common carotid, a hypoplastic left subclavian, and a hypoplastic and fibrotic right subclavian artery. The right subclavian originated adjacent to the left common carotid artery. The right common carotid artery was dissected into the neck but no definite subclavian vessel was encountered. The wall of the thoracic aorta was greatly increased in thickness, and numerous bright-yellow atheromatous deposits were found throughout its length. The abdominal aorta presented a marked degree of coarctation between the celiac axis and the renal arteries. A valvelike structure appeared at the level of the coarctation. Distal to the coarctation, the aorta narrowed to about one-fourth the caliber of the thoracic aorta, and in the coarctated segment the wall was thin. The thoracic aorta showed far more atheromata than was anticipated in a 12-year-old patient. There was evidence of chronic passive congestion in the lungs, liver, and spleen.

Microscopic Examination: The epicardium was thin and contained a definite increase in subepicardial fat. The cardiac myofibrils were enlarged and exhibited large hyperchromatic nuclei. A slight amount of interstitial edema and fibrous tissue was present. The valves were normal. Minimal intimal proliferation was present in the coronary arteries. In the thoracic and upper abdominal aorta there was extensive proliferation of the intima, in which were deposited cholesterol crystals and calcium. The media of the thoracic aorta was thickened and was undergoing early focal necrosis. Elastic stains revealed fragmentation of the internal elastic membrane, medionecrosis, and marked intimal proliferation. A section through the anomalous right subclavian artery revealed fibrous tissue throughout with no demarcation into layers. The lumen of this vessel was very small and presented a well-defined internal elastic membrane.

Anatomic Summary.—

The anatomic diagnoses were: (1) congenital coarctation of the abdominal aorta, (2) hypoplasia of the right subclavian artery with anomalous origin from the aorta, (3) hypoplasia of the left subclavian artery, (4) left ventricular hypertrophy, (5) focal chronic myocarditis, (6) arteriosclerosis of the aorta and great vessels proximal to the coarctation, (7) medionecrosis of the aorta, (8) bronchopneumonia, (9) pulmonary edema, (10) fatty liver, marked, (11) chronic passive congestion of the viscera.

DISCUSSION

The early reports of coarctation of the abdominal aorta from 1835 to 1929[1-4] consisted of unsuccessful attempts to correlate this lesion with syphilis and other diseases causing vascular disorders. In the later reports of Costa,[5] of Schleckat,[6] and of Maycock,[7] the congenital basis of the coarctation was strongly suspected. These authors arrived at their opinion after inflammatory and degenerative lesions were carefully considered and their possibility discarded. In the patient presented, the association of a congenital anomaly, the origin of the right subclavian artery from the aorta, with the abdominal aortic coarctation provides presumptive evidence for the congenital origin of the abdominal abnormality.

Proximal to the coarctation there was marked atherosclerosis and calcific arteriosclerosis. Stewart and Bellet[9] have shown that in coarctation of the thoracic aorta the hypertension proximal to the obstruction results in atherosclerotic vascular changes in this segment of the aorta. In this patient the marked atherosclerosis involved the aorta and to some extent the orifice of the left subclavian artery. This, associated with the stenosis of the right subclavian artery and the abdominal coarctation, resulted in a masking of the hypertension which

was present in the thoracic aorta and a portion of the abdominal aorta. The aortic hypertension proximal to the coarctation was sufficient to cause left ventricular hypertrophy and dilatation and finally congestive heart failure although hypotension existed in the extremities.

The surgical correction[10-13] of coarctation of the aorta and anomalies of the great vessels has necessitated accurate and early diagnosis of these lesions as their diagnosis is no longer solely of academic interest. Ordinarily the diagnosis of congenital coarctation of the abdominal aorta should not be difficult. The syndrome of abdominal bruit, diminished femoral pulsations, hypertension in the upper extremities, and absence of abdominal pain, should be strongly suggestive of this condition. Evidence of collateral circulation, such as pulsation of the lower intercostal arteries, may be helpful.[14] Useful information regarding the physical findings of this condition could not be gathered from the literature inasmuch as the diagnosis was not ordinarily established accurately ante mortem. In our patient the abdominal bruit was somewhat louder anteriorly than posteriorly, and was unaccompanied by a thrill. Ordinarily diminished femoral pulsations would be associated with hypertension in the upper extremities. In our patient, however, anomalies of the subclavian arteries and atherosclerosis interfered with the development of this sign. Pulsations of the lower intercostal arteries were a prominent physical finding. This was not, however, associated with notching of the ribs. This may have been due to the young age of the patient or to peculiarities in the development of the collateral circulation. Bramwell and Jones[15] reported thirteen patients with coarctation of the thoracic aorta associated with notching of the ribs. The youngest of their series is 11 years of age. Brown[16] states that notching of the ribs had been reported in patients as young as 6 years. It is possible that the location of the notching of the lower ribs, especially the tenth dorsal to the twelfth, may be of importance in the diagnosis of coarctation of the abdominal aorta. In coarctation of the thoracic aorta, notching is ordinarily present on the third to tenth ribs. The notching is usually posterior because of the fact that the main blood flow enters the intercostals by the lateral and dorsal branches, whereas the anterior intercostals arising from the internal mammary are comparatively unimportant. Notching is more prominent on the inner surface of the third to sixth ribs and on the outer surface of the sixth to tenth ribs. This may be due to slight differences in the position of the intercostal arteries where they leave the aorta in relation to the origin of the ribs. It is possible that congenital coarctation of the abdominal aorta gives a sufficiently different picture to be helpful in differential diagnosis. In this case, the position of the collateral pulsation in the region of the seventh and twelfth intercostal arteries was helpful in differentiating coarctation of the abdominal aorta from coarctation of the thoracic aorta. Briggs[14] has emphasized the inspection, palpation, and auscultation of the intercostal, intervertebral, abdominal, carotid, and femoral arteries as a part of a complete cardiovascular examination. Kerr[17] has utilized the symballophone in the ante-mortem diagnosis of abdominal aortic coarctation.

Other diagnostic procedures, such as the determination of the rate of blood flow to the upper and lower extremities, the impulse propagation time to the

upper and lower extremities, and comparative circulation times, as well as Diodrast injection, would aid in the diagnosis of this condition. Katz, Malinow, Kondo, Feldman, and Grossman[18] used Diodrast experimentally to outline the contour of the aorta.

Conditions which must be differentiated in making a diagnosis of congenital coarctation of the abdominal aorta are: aortic aneurysm, acute thrombosis of the abdominal aorta, the Leriche syndrome,[19] embolus to the abdominal aorta, arteriosclerosis in this region, dissecting aneurysm, primary or metastatic neoplasms, and medionecrosis.

It is believed that the differential diagnosis of cardiomegaly of unusual origin should include coarctation of the abdominal aorta along with such diseases as Gierke's disease, avitiminosis due to thiamine deficiency (B_1), adhesive pericarditis, myxedema heart disease, and mediastinopericarditis.

It should be noted that the coarctation was above the renal arteries and below the arteries supplying blood to the intestinal tract. It is conceivable that slight variations in the position of this coarctation would produce ischemia or infarction of organs below the coarctation. In our patient, the coarctation involved the orifice of the inferior mesenteric artery. There was no evidence of infarction of the gastrointestinal system, however. This is in keeping with the findings of others. The influence of renal ischemia on the presence of hypertension in this instance is not known.

From the therapeutic point of view the recognition of the reversible types of cardiac disease is important. Among these is heart disease due to: hyperthyrodism, avitaminosis due to thiamine deficiency (B_1), selected cases of syphilis, bacterial endocarditis, certain anemias, acquired or congenital arteriovenous fistulas, patent ductus arteriosus, tetralogy of Fallot, coarctation of the thoracic aorta, hypertension associated with chromaffin tumors, some types of renal ischemia, and other causes. Congenital coarctation of the abdominal aorta probably will take its place among those types of cardiac disease which are surgically reversible. The recognition of this condition may thus be lifesaving.

SUMMARY

The record of a patient who had congenital coarctation of the abdominal aorta, associated with anomalous origin of the right subclavian artery from the aorta, is presented. The importance of the ante-mortem diagnosis of congenital coarctation of the abdominal aorta is discussed. This condition may be classified theoretically as a surgically reversible type of congenital cardiac disease.

The authors are indebted to Doctor K. Tashiro and Doctor T. Murakami for assistance in this study.

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Selected Abstracts

Lasser, R. P., Rosenthal, N., and Loewe, L.: Death Following Use of Tetraethylammonium Chloride. J. A. M. A. **139**:153 (Jan.), 1949.

A 33-year-old white woman with marked essential hypertension underwent a two-stage thoracolumbar sympathectomy and splanchnicectomy which resulted in the disappearance of her headaches despite the absence of any significant lowering of the blood pressure. Six months after operation she was again hospitalized because of nausea, vomiting, rapidly progressive loss of vision, headache, epistaxis, and vaginal bleeding. The blood pressure was 220/100; the heart was enlarged; there was marked proptosis; and advanced hypertensive changes with hemorrhages and exudates were present on fundoscopic examination. The blood urea nitrogen was 78.4 mg. per cent and urinalysis revealed the presence of albumin and varying numbers of erythrocytes and leucocytes. A diagnosis of malignant hypertension was made.

In an effort to bring about a remission, 500 mg. of tetraethylammonium chloride (Etamon) in a total volume of 5.0 c.c. was administered by vein over a five-minute period. Within thirty minutes the blood pressure fell from 230/140 to 60/20, and cyanosis, dyspnea, and coma occurred. The patient died in shock six hours after the administration of the drug.

Inasmuch as tetraethylammonium chloride is excreted almost quantitatively by the urine, 50 per cent appearing in the first thirty minutes, the authors feel that the prolonged hypotensive effect of the drug in this patient can be explained by diminished excretion resulting from the renal damage which was present, and they emphasize the danger attendant upon the use of tetraethylammonium chloride in the malignant phase of essential hypertension.

HANNO.

Gross, R. E.: Surgical Treatment for Coarctation of the Aorta. J. A. M. A. **139**:285 (Jan.), 1949.

The author points out that because of the seriousness of the prognosis in coarctation of the aorta, surgical intervention is indicated. Only 26 per cent of a series of patients with this abnormality survived beyond middle age without more than moderate disability; the remainder succumbed to bacterial endocarditis or aortitis (22 per cent), rupture of the aorta (23 per cent), or the effects of the hypertensive state (28 per cent). The average age at death of patients dying from coarctation of the aorta or its complications was about 30 years.

The results of surgery in sixty patients with coarctation are reviewed. In six patients exploration only was done; end to end anastomosis was effected in fifty-two instances; and subclavian anastomosis was performed in two patients. Complete relief of hypertension resulted in forty-one patients, incomplete relief was obtained in five and no change in one. Seven operative and postoperative deaths occurred. In one patient, not included in the series, an aortic graft, 5.0 cm. in length, which had been preserved for thirty days, was used to effect an otherwise technically impossible end-to-end anastomosis; this child has been well after the first postoperative month.

The author states that surgery before the age of 6 to 8 years is not ordinarily desirable and that the risks of operation in patients beyond the teens are enhanced by the fibrosis and inelasticity of the aorta resultant from the long-standing hypertension.

HANNO.

Gasul, B. M., Glasser, J. M., and Grossman, A.: Extreme Hypertension in a Child Cured by Nephrectomy. J. A. M. A. **139**:305 (Jan.), 1949.

A 9-year-old girl with severe systolic and diastolic hypertension, complicated by hemorrhagic and exudative retinopathy, was found clinically to have a small nonfunctioning right kidney. Nephrectomy was performed and pathologic study revealed chronic pyelonephritis. The blood pressure fell to within normal limits by the tenth postoperative day. Re-examination two years after surgery disclosed a normal blood pressure, normal urinary findings, and no evidences of azotemia; fundoscopic examination revealed no abnormalities except for a number of small pigmentary lesions in the maculae.

The authors point out that unequivocal instances of hypertension as a result of unilateral renal disease are distinctly uncommon. They were able to cull from the literature only thirty-one cases (twenty-two in adults and nine in children) of hypertension in association with unilateral renal disease in which the blood pressure remained normal for a minimum of one year following nephrectomy.

HANNO.

Friedman, M., and Biné, R., Jr.: A Study of the Rate of Disappearance of a Digitalis Glycoside (Lanatoside C) From the Blood of Man. J. Clin. Investigation **28**:32 (Jan.), 1949.

These workers used a method for determining extremely minute amounts of a digitalis glycoside (lanatoside C) by means of the embryonic duck heart preparation. From previous work, it was found that the embryonic duck heart exhibited a "digitalis effect" (the occurrence of A-V block, missed beats, or bradycardia) when immersed in serum containing 0.10 microgram or more of lanatoside C per c.c. of blood. The time necessary for the occurrence of this digitalis effect varied inversely with the amount of glycoside present in the serum.

Serum samples from ten patients (seven of whom had congestive heart failure) and who had not received any digitalis therapy within three months were tested by the injection of 1.6 mg. of lanatoside C by vein over a three-minute period. Blood samples were obtained from the vein of the opposite arm immediately and for other determinations, within the first half hour.

The average concentration of the glycoside was 0.25 microgram per c.c. of serum; no significant difference was found in the serum concentration of the drug in patients with or without congestive failure. There was a rapid fall in serum concentration of digitalis glycoside so that by the end of fifteen minutes none was detectable in the sera of two of the ten patients and by the end of twenty-two and one-half minutes, the serum of only two of the eight patients tested still contained detectable amounts of the glycoside. Two patients experienced symptoms of digitalis intoxication twenty-four hours after administration at which time digitalis was detected in the serum.

From a previous study it was found that little or none of the glycoside is absorbed or contained in the red cells and that the plasma proteins are not able to absorb this particular glycoside. Furthermore, it had been shown by these investigators that serum itself does not inactivate lanatoside C and it seems most likely that the escape of the glycoside from the blood stream is by the simple process of diffusion.

WAIFE.

Reubi, F. C., and Schroeder, H. A.: Can Vascular Shunting be Induced in the Kidney by Vasoactive Drugs? J. Clin. Investigation **28**:114 (Jan.), 1949.

These experiments were made in order to detect changes in the route of blood supply of the different parts of the nephron after the administration of certain drugs. It was believed that the opening or closing of anastomotic channels between arteries and veins, such as has been suggested by Trueta and his group, would be reflected by relative changes in the renal extraction of *p*-amino hippurate and/or mannitol, the utilization of oxygen, or both. Fourteen patients, including eight with arterial hypertension, underwent catheterization of the right renal vein. In addition, fifteen dogs were similarly studied. Determinations were made before and after injection of epinephrine, histamine, and Pentothal.

It was found that the maximal decrease in the extraction of PAH by the kidneys of patients after subcutaneous epinephrine or histamine was 11.4 per cent. Dog experiments were inconclusive. Similarly, arteriovenous oxygen differences were inconstant, being increased by epinephrine in two and decreased in three.

In dogs, the oxygen capacity, hematocrit and plasma protein content were more concentrated in the renal vein than in the renal artery. This difference was increased by epinephrine. It is suggested that this loss of fluid from renal blood may have occurred through renal lymphatic vessels or through other vascular channels.

It is concluded that large intermittent shunts were not demonstrated in man by physiological doses, or in dogs by larger doses, of epinephrine. In patients with essential hypertension, histamine or epinephrine produced small and inconsistent changes which could be ascribed to the presence of shunts.

WAIFE.

Christensen, L. R.: Methods for Measuring the Activity of Components of the Streptococcal Fibrinolytic System, and Streptococcal Desoxyribonuclease. J. Clin. Investigation **28**:163 (Jan.), 1949.

This is a report of methods used for the quantitative estimation of streptokinase (streptococcal fibrinolysin) antistreptokinase (antifibrinolysin), serum inhibitor (serum trypsin inhibitor), serum plasminogen (serum fibrinolysin), and desoxyribonuclease.

In a survey of various sera, it was found that there was a marked rise in antistreptokinase activity following intrapleural injection of streptokinase in human beings. Serum from the normal adult contains more antistreptokinase than that of an infant and this level is strikingly high in rheumatic fever. Species differences in concentrations were noted.

The serum inhibitor levels show elevations in wasting diseases, and among animals the guinea pig has an exceptionally high inhibitor titer. It also appears that plasminogen levels are increased in tuberculosis.

WAIFE.

Lubschitz, K., Lundrsteen, E., and Forchhammer, E.: Primary Malignant Heart Tumor Diagnosed in Vivo With the Aid of Artificial Pneumopericardium. Radiology **52**:79 (Jan.), 1949.

In a review of the literature, these authors were able to find only 163 instances of primary heart tumors reported up to 1945. In only twelve of these had the diagnosis been made in vivo.

The authors present the case of a young woman, 23 years old, with symptoms of severe cardiac decompensation. Adequate treatment had very little effect on the cardiac decompensation even after considerable quantities of pericardial fluid had been evacuated. Following pneumopericardium, the heart was seen to be of approximately normal size, and a soft tissue mass was seen projecting along the right border of the heart. Following repeated aspirations, tumor cells were isolated from the pericardial exudate. At necropsy, a hemangioendotheliosarcoma was found arising from the right atrium, filling the latter and extending through the tricuspid valve into the right ventricle. The symptomatology of a heart tumor is frequently that of cardiac decompensation which develops without demonstrable cause and is refractory to treatment. A pericardial effusion is found in about one-half the patients and is almost always bloody. Electrocardiograms have been described showing cardiac infarction, bundle branch block, sinoauricular and atrioventricular block, Stokes-Adams syndrome, etc.

The x-ray findings frequently reveal an enlarged heart which in most instances is not characteristic of a specific etiology. A rapid increase in cardiac size on serial roentgen studies should arouse the suspicion of the possibility of a cardiac tumor. If this is due to an effusion, the induction of a pneumopericardium may give valuable information.

ZION.

Wangensteen, O. H., Varco, R. L., and Baronofsky, I. D.: The Technique of Surgical Division of Patent Ductus Arteriosus. Surg., Gynec. & Obst. **88**:62 (Jan.), 1949.

There is no complete unanimity among surgeons that division of the ductus is preferable to ligation. The basis of this difference in attitudes is that mere ligature is a simpler and safer operation than division; otherwise, everyone would agree that division is the surer operation from the standpoint of avoidance of recanalization.

The authors present a series of sixty-nine consecutive cases in all of which operative division of the ductus was performed. While complications developed in some of the sixty-nine cases there was only one death in the series. This occurred in a patient of 31 years with subacute bacterial endocarditis, auricular fibrillation, and severe cardiac decompensation, in whom a granulomatous plaque beneath the pulmonic end of a broad ductus made ligature difficult after division of the ductus. A technique for dissection and division of the ductus, consisting essentially of the technique described by Gross, is presented.

BECK.

Horns, H. L.: Hemochromatosis. Am. J. Med., **6**:272 (Feb.), 1949.

Although hemosiderin deposition of severe degree within the muscle fibers of the heart is a frequent autopsy finding in cases of hemochromatosis, cardiac symptoms are not prominent in the clinical picture of this disease. However, the recent literature has described nine cases of hemochromatosis in which cardiac symptoms have been prominent. The author describes a patient with severe hemochromatosis, including a history of attacks of severe precordial pain followed in a few months by mild exertional dyspnea, orthopnea, and slight ankle edema. During hospitalization it was noted that there was left ventricular enlargement by x-ray. Electrocardiograms showed low QRS voltage with isoelectric T_1 and questionably diphasic T_2. Later T_1 and T_2 became definitely diphasic. The patient showed evidence of increasing cardiac decompensation with massive edema of the legs and scrotum, shifting dullness in the flanks, and scattered râles in the lung bases. The patient's edema progressively increased in spite of treatment with digitalis, low salt diet, and mercurial diuretics.

At autopsy there was fluid in the abdominal and both pleural cavities. The heart weighted 440 grams, the ventricular walls were hypertrophied and there was some dilatation of the left ventricle. The valves were normal, the coronary arteries showed no evidence of arteriosclerosis, and the aorta was normal. Microscopically the muscle fibers of the heart were pale-staining with fragmentation in some areas. There was an increase in the spaces between the fibers. The muscle fibers were heavily infiltrated with pigment staining blue with ferrocyanide. The other organs showed the ordinary findings of hemochromatosis.

SCHWARTZ.

Dotter, C. T., and Steinberg, I.: Angiocardiographic Study of the Pulmonary Artery. J. A. M. A. **139**:566 (Feb.), 1949.

As opposed to the difficulty and inadequacy of visualizing the pulmonary artery by conventional roentgenography, accurate and precise visualization of the pulmonary artery and its branches is afforded by angiocardiography. This paper sets forth the changes brought out by this method in the configuration of the pulmonary artery in various congenital and acquired cardiac disorders.

Dilatation of the pulmonary artery was well demonstrated by this method in cases of patent ductus arteriosus, septal defects, the Eisenmenger complex, pulmonic stenosis, idiopathic aneurysmal dilatation, mitral stenosis, congestive failure, chronic pulmonary disease, and kyphoscoliosis. In the tetralogy of Fallot, angiocardiography serves to establish unequivocally the diagnosis, to rule out the clinically similar Eisenmenger syndrome, and, by demonstrating the exact anatomic deformity present, to aid the surgeon in correctly planning his operation. Angiocardiography is also of aid in the differentiation of vascular hilar and mediastinal lesions from neoplasms.

HANNO.

Neuhof, H., Sussman, M. L., and Nabatoff, R. A.: Angiocardiography in the Differential Diagnosis of Pulmonary Neoplasms. Surgery **25**:178 (Feb.), 1949.

The authors attempted to apply angiocardiography to the differential diagnosis of the various types of pulmonary neoplasm. In the case of malignant tumors of main bronchi, the large pulmonary vessels in the area of the neoplasm were found to be partially or completely occluded. In the malignant tumors of small or branch bronchi, similar findings were obtained. In the case of benign, slowly expanding lesions, the vessels were found to be displaced and surrounding the tumor, but they were intact. Mediastinal and pleural lesions caused no significant change in the angiogram.

ABRAMSON.

Cooper, F. W., Jr., Robertson, R. L., Shea, P. C., Jr., and Dennis, E. W.: The Experimental Production of Gradual Occlusion of Large Arteries With Polythene and Tantalum. Surgery **25**:184 (Feb.), 1949.

An experimental procedure is described for the production of a gradual and complete occlusion of large arteries in dogs, using a combination of a tantalum band to initiate a partial occlusion, and polythene to produce a perivascular reaction. By utilizing both substances, it was possible to use smaller quantities of polythene, to produce a more rapid occlusion of the vessel, and to reduce the extent of the perivascular reaction.

ABRAMSON.

Currens, J. H., and White, P. D.: Cough as a Symptom of Cardiovascular Disease. Ann. Int. Med. **30**:528 (March), 1949.

Cough may have a psychogenic cause and, therefore, may occur in cases which manifest the usual stigmata of a cardiac neurosis. It may also be a predominant and early symptom in various types of organic cardiovascular disease. In the latter group it usually results from cardiac failure or from mechanical pressure. The authors describe patients with rheumatic, thyrotoxic, hypertensive, and syphilitic heart disease in whom cough was the presenting symptom because of cardiac decompensation. They also include examples of syphilitic aneurysm, congenital right-sided aortic arch, and constrictive pericarditis to illustrate how mechanical pressure can be responsible for the symptom.

WENDKOS.

Gerber, I. E., and Mendlowitz, M.: Visceral Thrombophlebitis Migrans. Ann. Int. Med. **30**:560 (March), 1949.

As a rule, this disease is characterized by involvement of short segments of medium- and small-sized vessels. In the more severe forms, however, long segments or complete venous systems may be involved with sequelae dependent upon the venous system attacked. More commonly, the veins of the lower extremities are affected and the inflammation wanders from one extremity to the other. The majority of cases are benign with localization of the disease process to the veins of the upper and lower extremities and occasional lesions in the visceral veins. Generally, the thrombi in the affected veins undergo organization and recanalization and except for minor sequelae, such as postural edema when the lower extremities are involved, there are no residua. Even those patients with occasional lesions in the visceral veins may go on to complete healing. There are no pathological features which permit specific characterization of migratory thrombophlebitis as either venous or perivenous in origin. Both types of inflammation are seen and the degree varies from case to case. The pathogenesis of thrombophlebitis migrans remains completely unclear. Inasmuch as recovery in thrombophlebitis migrans is common, nonspecific supportive therapy should always be maintained.

WENDKOS.

Leaman, W. G., Wikingsson, M. B., Webster, M. B., and Shaw, C. C.: Caronamide and Penicillin in Subacute Bacterial Endocarditis Due to Streptococcus Faecalis. Ann. Int. Med. **30**:646 (March), 1949.

A 25-year-old Negro woman, with mitral stenosis, developed subacute bacterial endocarditis approximately seven days following delivery. The nidus of infection was apparently an endometritis. The offending organism was a resistant type of *Streptococcus faecalis* which was isolated upon culture of the lochia and from the patient's blood stream. The organism was resistant to 1 million units of penicillin daily, but responded promptly to 4.0 Gm. of streptomycin per day. One week following withdrawal of streptomycin, there was a recrudescence of infection as shown by repeatedly positive blood cultures. The organism was then found to have developed increased penicillin resistance. This was overcome by the co-administration of oral Caronamide (24 Gm.) and intramuscular aqueous penicillin (4 million units per day). Blood samples were obtained at appropriate intervals during this therapeutic regimen to demonstrate the action of Caronamide in enhancing the concentration of penicillin in the plasma when compared with plasma levels of antibiotic when equal doses of penicillin alone were administered. Caronamide plasma concentrations were also determined. The patient reported herein, tolerated a daily dose of 24 Gm. of Caronamide for sixty-six consecutive days without tubular epithelial damage or renal impairment. Adequate penicillin plasma levels during this period resulted in sterilization of the patient's blood stream and an apparent clinical arrest of her disease.

WENDKOS.

Sampson, M. C., Eissler, K. R., and Nay, R. M.: Polyarteritis Nodosa: A Report of an Unusual Case. Ann. Int. Med. **30**:668 (March), 1949.

A 26-year-old man was first admitted to the hospital because of the sudden onset of a right-sided hemiparesis associated with a slurred speech and numbness of the right arm, right leg, and right side of the face. Since the age of 16 he had suffered from repeated bouts of polyarthritis, fever, and transient subcutaneous nodules. At the age of 21, evidences of nephritis were discovered. Physical examination at the time of admission revealed signs indicative of widespread patchy involvement of the central nervous system. No significant eosinophilia was observed in the peripheral blood. Urinalysis revealed evidences of renal disease and renal impairment. During a two-month period of hospitalization, the neurological findings gradually disappeared and several crops of cystic subcutaneous nodules made their appearance. Biopsy of one of these nodules revealed changes in the blood vessels traversing the areolar tissue which were compatible with a diagnosis of polyarteritis nodosa.

WENDKOS.

Cole, S. L.: Tap Water Sodium in the Low Sodium Diet. J. A. M. A. **140**:19 (May), 1949.

This paper points out that the sodium content of drinking water is a factor to be considered when a salt-poor regimen is instituted in the treatment of heart failure, hypertension, or renal disease. Tap water high in sodium may nullify the effects of a stringent low salt diet. In a number of cities (Los Angeles, Houston, Phoenix, etc.) the sodium level of tap water is in excess of 10 mg. per hundred cubic centimeters. The concentration of sodium may be increased by the softening processes in the various institutions in which the water is used. It is suggested that distilled, deionized, or spring water be used in conjunction with a low sodium diet in areas where the tap water shows a high sodium concentration.

HANNO.

Announcement

IMPORTANT NOTICE CONCERNING PAPERS OFFERED FOR PRESENTATION AT THE INTERNATIONAL HEART CONGRESS IN PARIS, SEPT. 3-9, 1950

It has been decided by the International Cardiac Council that titles and summaries (not exceeding 300 words) of papers offered for presentation at the First International Heart Congress in Paris next September should be sent to the Secretary of each national heart association throughout the world. A Committee of the American Heart Association has already been established to select the most suitable communications from the U. S. A. to be forwarded to the Inter-American Cardiac Committee and thence to the headquarters in Paris where final selection will be made. The listing submitted by the American Heart Association Committee will be arranged on a priority basis. It is expected that 400 to 500 papers may be read at the meeting in Paris and that half of these will be allocated to the Western Hemisphere. Each communication is to take not over ten minutes as a rule followed by a five minute discussion period. These titles and summaries should be in the hands of Dr. Charles A. R. Connor, Medical Director, American Heart Association, 1775 Broadway, New York, N. Y. by March 1.

SECRETARY PRO TEM

INTERNATIONAL CARDIAC COUNCIL